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Association of novel serum biomarkers (Oncostatin M, 90K/Mac-2 BP, and IL-12 p40) with adalimumab target trough level achievement and response in Iraqi inflammatory bowel disease patients: A cross-sectional real-world study

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Abstract

Fecal calprotectin, fecal lactoferrin, and C-reactive protein are well-established biomarkers of inflammatory bowel disease (IBD) activity. This study explores novel serum biomarkers, including Oncostatin M (OSM), 90K/Mac-2 binding protein (90K), and interleukin (IL)-12 p40, and their possible association with the achievement of target adalimumab (ADL) trough level (TL) and with clinical response among 88 Iraqi adult patients with IBD. In this cohort, serum OSM was significantly higher in patients who failed to achieve the target adalimumab TL (median 198.61 pg/ml, IQR 139.57–276.86) compared to those who did (median 134.61 pg/ml, IQR 108.47–192.71; $p = 0.004$). In multivariate logistic regression, each 1 pg/ml increase in OSM raised the odds of not achieving the target TL (OR 1.007; 95% CI 1.002–1.013; $p = 0.006$). Notably, OSM did not differentiate patients in clinical remission from those with active disease ($p > 0.05$). Similarly, serum 90K and IL-12 p40 showed no significant differences between patient groups stratified by TL achievement or disease activity. In conclusion, serum OSM levels were significantly higher in patients failing to achieve adalimumab target trough levels and were significantly associated with adalimumab TL achievement in this Iraqi cohort, demonstrating the feasibility of serum OSM measurement in a real-world clinical setting.

Keywords

adalimumab, inflammatory bowel disease, IL-12p40, Oncostatin M, 90K/Mac-2 binding protein

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PENSOFT

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory gastrointestinal disorder that generally requires lifelong medication and is associated with considerable morbidity, hospitalization needs, and productivity losses (Yeshi et al. 2024). Based on symptoms, disease location, and histopathological characteristics, IBD comprises two main phenotypes (Fadhil et al. 2019; Saez et al. 2023): ulcerative colitis (UC), which is typically restricted to the colon and rectum (Liu et al. 2023), and Crohn's disease (CD), which can affect the entire gastrointestinal tract (Nawar Abdulridha et al. 2024).

Inflammatory bowel disease has a complex, incompletely understood etiology. The currently available evidence suggests that IBD results from multifactorial interactions between environmental factors and genetically susceptible individuals, mediated by the gut microbiota, that precipitate abnormal intestinal immune responses, ultimately resulting in tissue damage and persistent inflammation (Jebur et al. 2018; Wan et al. 2025). T-helper (Th) cell responses are the main cause of this inflammatory environment, with Th1 and Th17 cells particularly implicated in CD and UC, respectively. Upon activation, these cells produce pro-inflammatory cytokines that prolong inflammation and tissue damage (Calvez et al. 2025).

Well-established biomarkers for IBD activity evaluation include C-reactive protein, fecal lactoferrin, and fecal calprotectin (Durham et al. 2025). Recent advances in IBD biomarker research have identified promising novel serum biomarkers such as Oncostatin M (OSM), 90K/Mac-2 binding protein (90K/Mac-2 BP), and interleukin (IL)-12 p40 (Pesole et al. 2023; Yang et al. 2024; Zhang et al. 2024). OSM belongs to the interleukin-6 family of proinflammatory cytokines and is produced primarily by hematopoietic cells such as T lymphocytes, dendritic cells, macrophages, neutrophils, and mast cells. It is a pleiotropic cytokine that is involved in the inflammatory process (Yang et al. 2024) and is a validated biomarker for predicting anti-TNF therapy failure in European and North American IBD cohorts. The expression of OSM is increased in the inflamed mucosa of patients with IBD and is closely associated with treatment-refractory disease (Cineus et al. 2025). In one cohort of more than 200 patients with IBD, those with elevated baseline OSM and OSM receptor expression showed a reduced infliximab response rate from 69–85% to only 10–15% (West et al. 2017). Although OSM is a promising biomarker for diagnosis and disease monitoring in patients with IBD, its predictive value for treatment response remains limited (Saleh et al. 2025).

Galectin-3-binding protein (90K/Mac-2 BP), or simply 90K, is a member of the Scavenger Receptor Cysteine Rich superfamily, which encompasses proteins largely implicated in host defense processes. 90K functions within the immunological and inflammatory response network that drives the stimulation of the host immune defense mechanisms, as demonstrated by the association between the concentrations of 90K and other cytokines (Pesole et al. 2023).

Among the many cytokines, IL-12 and IL-23 were thought to be key drivers of intestinal inflammation through significant effects on innate or adaptive immunity. They share a component called IL-12p40, encoded by the IL12B gene, which is a central cytokine of the IL-12/23 pathway and is essential to the development of chronic intestinal inflammation (Wang et al. 2015; Verstockt et al. 2023). The expression of IL-12p40 was increased both systemically and locally in patients with IBD but was significantly higher in patients with CD. Additionally, IL-12p40 signaling was found to have a key effect on the functions of human CD4+ T cells, a mechanism implicated in IBD pathogenesis (Wang et al. 2015).

One of the treatment options for IBD is anti-TNF medications, which inhibit TNF activity and are utilized when other treatments fail to control disease activity (Mohammed et al. 2020). Infliximab, adalimumab (ADL, a subcutaneous fully humanized IgG1 monoclonal antibody), golimumab, and certolizumab pegol are TNF-α inhibitors that have been employed in the clinical setting of IBD; each has a distinct pharmacological profile and varying efficacy (Gareb et al. 2020; Lichtenstein et al. 2025). For IBD, the standard ADL regimen is a dose of 160 mg at week 0 (day 1), then 80 mg 2 weeks later (day 15), then 40 mg subcutaneously every 2 weeks (beginning week 4, day 29) as maintenance (Savelkoul et al. 2023). The recommended maintenance ADL target trough level (TL) for IBD is 8–12 μg/mL (Irving and Gecse 2022). The association of OSM, 90K, and IL-12p40 with adalimumab trough level achievement, a distinct pharmacokinetic outcome, has not been comprehensively examined in real-world therapeutic drug monitoring contexts, especially in Iraq or the West Asia region, despite known regional differences in IBD phenotypes and genetics.

The current study aims to determine the possible association between levels of novel biochemical markers (OSM, 90K, and IL-12p40) and both the achievement of the target serum TL of ADL and ADL responsiveness among Iraqi patients with IBD.

Patients and methods

Study design and setting

The current study employed a cross-sectional observational design and was conducted at the Gastroenterology and Hepatology Teaching Hospital, Medical City, Baghdad, Iraq, from April 2024 to November 2024. All patients were under the supervision of a specialist gastroenterologist and were managed in accordance with clinical guidelines (Raine et al. 2022; Gordon et al. 2024).

Inclusion criteria

The inclusion criteria for the current study were:

1. IBD patients of either sex over 18 years of age.
2. Ulcerative colitis patients with moderate or severe disease according to the Truelove and Witts' severity index (National Clinical Guideline 2013) who were on standard maintenance therapy, which included ADL (40 mg SC every 2 weeks (Vulliemoz et al. 2020)) + azathioprine + 5-aminosalicylic acid for more than 3 months.
3. Crohn's disease patients who had been diagnosed with moderate to severe disease based on the European Crohn's and Colitis Organization definitions of disease activity (Peyrin-Biroulet et al. 2016) and who were on standard maintenance therapy, which included ADL (40 mg SC every 2 weeks (Vulliemoz et al. 2020)) + azathioprine for more than 3 months.

Exclusion criteria

Patients with the following comorbid conditions—rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and systemic lupus erythematosus—were excluded because these immune system diseases may impact biomarker blood levels and may serve as indications for corticosteroid or anti-TNF therapy. Additional exclusions included patients who had received an organ transplant; had diabetes mellitus, asthma, chronic obstructive pulmonary disease, or severe cardiovascular, hepatic, or renal illnesses; were undergoing cancer therapy; or had used systemic or rectal steroids during the last 8 weeks.

Study groups

The total sample size of eligible adult patients with IBD (CD and UC) was 88 in the current study. We enrolled consecutive eligible patients with IBD presenting to the hospital during the study period via convenience sampling after obtaining verbal informed consent. This sampling method was chosen due to the complexity of identifying and recruiting eligible patients meeting strict inclusion and exclusion criteria and pragmatic constraints, including limited resources and the need for timely completion. The patients were divided into two main groups according to their TL achievement and disease activity: Group 1 includes patients with IBD who reached the ADL target TL of 8–12 µg/mL. Group 2 includes patients who did not reach the ADL target TL. Assessment of patient response (by physician) was done using the CDAI score for CD (remission: <150; active disease: ≥150) (Peyrin-Biroulet et al. 2016) and the Partial Mayo Score for UC (remission: <2; active disease: ≥2) (The Italian Group for the study of Inflammatory Bowel Disease 2023).

Data collection

Demographic and clinical data (age, sex, body mass index (BMI), length of disease, prior biological therapy) were collected via a patient data sheet created specifically for this study through direct patient interviews.

Sample preparation and laboratory parameters

A 5 ml venous blood sample was collected from each patient, allowed to clot, and centrifuged for 20 minutes at 2,000–3,000 rpm. Serum samples were separated from the resulting supernatant, stored in Eppendorf tubes, and preserved in a deep freezer at −80 °C until the time of biomarker analysis. The TL of ADL from Matriks Biotek [Turkey (Cat. ADA-SPEC-ADA), detection limit (sensitivity) (ng/mL): 18.75, spike recovery (%): between 85 and 115, precision: intra-assay and inter-assay CVs <30%]; human OSM from Feiyue Biotechnology [China (Cat. No. FY-EH3747), detection limit (sensitivity): 9.38 pg/mL, recovery (%): between 80 and 120, precision: intra-assay and inter-assay CVs <10%]; human 90K from Fine Test Biotech [China (Cat. No. EH1761), detection limit (sensitivity): 0.75 ng/ml, recovery (%): between 88 and 102, precision: intra-assay and inter-assay CVs <10%]; and serum human IL-12p40 from Fine Test Biotech [China (Cat. No. EH0175), detection limit (sensitivity): 18.75 pg/ml, recovery (%): between 86 and 101, precision: intra-assay and inter-assay CVs <10%] were measured by the ELISA test. These tests were conducted using the sandwich type as the guiding premise, which are plate-based assays for detecting and quantifying a specific protein in a complex mixture. Concisely, standards and serum samples are incubated in the microtiter plate pre-coated with the human monoclonal anti-ADL antibody for ADL detection and pre-coated with either human anti-OSM, anti-90K, or anti-IL-12p40 antibodies for OSM, 90K, and IL-12p40 detection, respectively. Standards and serum samples are added, bound to antibodies coated on the wells, and are then incubated. After incubation, unbound conjugates are removed with a wash buffer. Then, only for OSM, 90K, and IL-12p40 detection, a biotinylated detecting antibody is added to bind with OSM, 90K, and IL-12p40 conjugated on the coated antibody. After washing off unbound conjugates, HRP-Streptavidin is added and binds to ADL, OSM, 90K, and IL-12p40. Following incubation, the wells are washed, and the bound enzymatic activity is detected by the addition of the tetramethylbenzidine chromogen substrate. To end, the reaction is terminated with an acidic stop solution. The color developed is proportionate to the amount of free ADL, OSM, 90K, and IL-12p40 in the sample or standard. The wavelength at which the absorbance was measured was 450 nm. After that, the proportional measurement of concentration in the samples was determined using the standard curve (Feiyue Biotechnology 2023; Wuhan Fine Biotech Co 2023a, b; Matriks Biotechnology 2025).

Statistical analysis

Normality was assessed using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation, while variables that are not normally distributed are presented as median and interquartile range (IQR). When the variables had a normal distribution, the

difference between the group of patients with IBD who reached the target TL of ADL and the group who did not reach it was evaluated using an independent t-test; if the data did not have a normal distribution, a Mann–Whitney U test was used. ROC curve analysis was performed to evaluate the biomarker potency of serum OSM. Binary logistic regression analysis was utilized to determine the relationship between various factors and TL attainment. All statistical analyses were performed using SPSS 27 (Chicago, USA), and *p*-values less than 0.05 were considered significant.

Results

Table 1 shows the characteristics of 88 patients with inflammatory bowel disease enrolled in the study, equally distributed between UC (n = 44) and CD (n = 44). Fifty-five patients (63.64%) were male. The age range was 18–65 years, and 31 patients (35.22%) had been previously treated with biologic exposure. Moreover, forty-seven patients (53.41%) reached the ADL target TL, while 41 (46.59%) did not, and 44 patients (50.0%) were in remission, while 44 patients (50.0%) had active disease.

Table 2 shows the difference between patients with IBD who reached the target TL of ADL (Group 1) and patients who did not reach it (Group 2) according to the levels of biomarkers. OSM levels were significantly higher in patients not achieving target levels (Group 2), while there were no statistically significant differences between groups regarding 90K and IL-12p40 levels.

Table 3 shows that, using univariate binary logistic regression, only OSM has a significant effect on reaching the ADL target TL. While multivariate binary logistic regression (backward technique) includes OSM, 90K, and IL-12p40 biomarkers and other clinical covariates for patients with IBD, only OSM had a statistically significant effect (negative association) on reaching the ADL target TL.

ROC curve analysis was performed to evaluate the discriminatory ability of serum OSM for predicting the non-achievement of the adalimumab target trough level (Fig. 1). The area under the curve (AUC) was 0.680 (95% CI: 0.567–0.792), indicating modest or fair discriminatory performance. An optimal OSM cutoff of 197.002 pg/mL provided a sensitivity of 0.537 (53.7%) and a specificity of 0.809 (80.9%).

Table 4 shows the difference between patients with IBD in remission and those with active disease, and there were no statistically significant differences between the two groups regarding all variables.

Table 5 shows response association and prediction by univariate and multivariate regression analysis for patients with IBD; only 90K and BMI remained in the final step of multivariate binary logistic regression (backward), and there were no statistically significant differences regarding all variables.

Table 1. Characteristics of inflammatory bowel disease patients who participated in the study.

Variables		IBD patients (N = 88)
Sex	Female [n (%)]	32 (36.36%)
	Male [n (%)]	56 (63.64%)
Age (year) [median ± IQR], Range (year)		32.50 (25.00–44.50), (18–65)
BMI (kg/m^2) [mean ± SD]		25.270 ± 5.163
Duration of disease (year) [median ± IQR]		7.00 (4.00–9.00)
No. of adalimumab doses [median ± IQR]		71.50 (36.00–110.00)
Biological treatment	Naive [n (%)]	57 (64.78%)
	Previous biological treatment. [n (%)]	31 (35.22%)
IBD type	UC [n (%)]	44 (50%)
	CD [n (%)]	44 (50%)
Patients' TL achievement	Reached TL [n (%)]	47 (53.41%)
	Not reached TL [n (%)]	41 (46.59%)
Response	Remission [n (%)]	44 (50%)
	Active [n (%)]	44 (50%)

BMI: body mass index; **CD**: Crohn's disease; **IQR**: interquartile range; **IBD**: inflammatory bowel disease; **SD**: standard deviation; **TL**: trough level; **UC**: ulcerative colitis.

Table 2. Difference between IBD patients who reached TL of ADL (Group 1) and patients who did not reach it (Group 2) according to the levels of the three biomarkers.

Variable	Group 1 (reached TL) (47 Patients)	Group 2 (did not reach TL) (41 Patients)	*P*-value
OSM (pg/mL)	134.61 (108.47–192.71)	198.61 (139.57–276.86)	0.004*[b]
90K (ng/mL	2291.604 ± 520.301	2125.775 ± 503.164	0.134[a]
IL-12 p40 (pg/ml)	7.951 (0.251–271.361)	25.628 (1.154–213.431)	0.515[b]

(*) Significant difference ($p < 0.05$). (**a**) A two-sample t-test was used, and the data are presented as mean ± **SD**. (**b**) The Mann–Whitney U test was used, and the data are presented as median (**IQR**). **OSM**: Oncostatin M; **TL**: trough level.

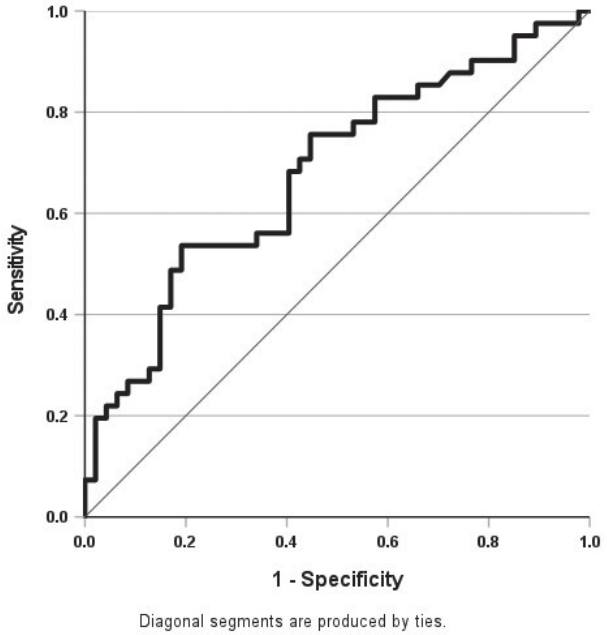


Figure 1. ROC curve analysis of serum OSM (AUC = 0.680 and $p = 0.004$).

Discussion

Individual biomarkers show limited utility in evaluating the therapeutic response in patients with IBD, and a new focus on multi-parametric models incorporating multiple biomarkers offers the most promising path toward a predictive solution (Dragoni et al. 2021; Privitera et al. 2021).

Results of the current study showed that serum OSM levels were significantly higher in patients with IBD who did not reach the target TL for ADL. Notably, OSM levels showed no significant difference between patients in remission compared to patients with active disease. These results agree with a previous study that demonstrated that plasma OSM levels were significantly elevated in participants with UC and CD who did not achieve remission at one year compared to participants who did. In the end, high OSM concentrations were linked to both UC and CD patients stopping anti-TNF and using corticosteroids more frequently. Accordingly, OSM may be a significant biomarker of the anti-TNF response (Guo et al. 2022). A meta-analysis in 2024 found significantly higher OSM levels in non-responders than in responders; higher OSM expression or levels are correlated with worse IBD outcomes and poor prognosis and concluded that OSM can be used as a surrogate marker for predicting poor prognosis in patients with IBD treated with anti-TNF therapies (Yang et al. 2024). The observed dissociation between OSM's association with adalimumab trough levels and its lack of association with clinical disease activity warrants careful interpretation. Adalimumab trough levels represent pharmacokinetic exposure, while clinical remission reflects the integrated pharmacodynamic response influenced by multiple factors beyond drug concentration. Studies demonstrate that about 20–40% of patients with IBD with adequate trough levels fail to achieve remission, indicating that drug exposure alone is insufficient for therapeutic success (Papamichael et al. 2015; Vulliemoz et al. 2020; Orfanidou et al. 2024).

Table 3. Association and prediction of reaching the target TL of ADL by the three biomarkers and other clinical covariates for IBD patients.

Variable	Univariate analysis [a]			Multivariate analysis [b]		
	OR [EXP (B)]	95% CI EXP(B) Lower-upper	*P*-value	OR [EXP (B)]	95% CI EXP(B) Lower-upper	*P*-value
OSM (pg/mL)	1.007	1.002–1.013	0.006*	1.007	1.002–1.013	0.006*
90K (ng/mL)	0.999	0.998–1.001	0.135	0.999	0.998–1.000	0.149
IL-12 p40 (pg/ml)	1.000	1.000–1.000	0.470	1.000	1.000–1.000	0.994
Age (year)	1.007	0.974–1.042	0.670	1.016	0.980–1.054	0.382
Sex	0.982	0.411–2.346	0.968	0.999	0.370–2.702	0.999
BMI (kg/m^2)	0.976	0.899–1.060	0.564	0.978	0.886–1.079	0.657
Duration of disease (year)	1.017	0.914–1.131	0.760	1.019	0.899–1.155	0.774
Prior biological treatment	0.895	0.372–2.149	0.803	1.095	0.366–3.280	0.871
No. of adalimumab doses	0.997	0.988–1.006	0.454	0.995	0.986–1.005	0.372
IBD type (UC, CD)	1.096	0.474–2.533	0.831	0.729	0.276–1.924	0.524

(*) Significant difference. (a) Binary logistic regression was used (Enter method). (b) Binary logistic regression was used (backward method). **BMI**: body mass index; **CI**: confidence interval; **IL**: interleukin; **OR**: odds ratio; **OSM**: Oncostatin M.

Table 4. Difference between IBD patients in remission and those with active disease according to the levels of the three biomarkers.

Variable	Remission (44 Patients)	Active disease (44 Patients)	*P*-value
OSM (pg/ml)	173.014 (112.604–215.671)	166.501 (115.989–222.634)	0.570[b]
90K (ng/mL)	2302.118 ± 486.050	2126.568 ± 535.819	0.111[a]
IL-12 p40 (pg/ml)	9.992 (1.063–265.927)	10.365 (0.341–199.398)	0.943[b]

(*) Significant difference ($p < 0.05$). (**a**) A two-sample t-test was used, and the data are presented as mean ± SD. (**b**) The Mann–Whitney U test was used, and the data are presented as median (interquartile range). **IL**: interleukin; **OSM**: Oncostatin M.

Table 5. Response association and prediction by univariate and multivariate analysis for IBD patients.

Variable	Univariate analysis [a]			Multivariate analysis [b]		
	OR [EXP (B)]	95% CI EXP(B) Lower-upper	P-value	OR [EXP (B)]	95% CI EXP(B) Lower-upper	*P*-value
OSM (pg/mL)	1.003	0.998–1.007	0.267			NS
90K (ng/mL	0.999	0.998–1.000	0.114	0.999	0.998–1.000	0.107 NS
IL-12p40 (pg/ml)	1.000	1.000–1.001	0.378			NS
Age (year)	1.001	0.968–1.035	0.966			NS
Sex	1.484	0.619–3.555	0.376			NS
BMI (kg/m^2)	0.924	0.848–1.006	0.070	0.922	0.845–1.005	0.065 NS
Duration of disease (year)	0.964	0.866–1.073	0.499			NS
Prior biological treatment	0.606	0.250–1.465	0.266			NS
No. of adalimumab doses	0.997	0.988–1.006	0.489			NS
IBD type (UC, CD)	1.000	0.434–2.307	1.000			NS

NS, non-significant difference ($p > 0.05$); (**a**) Binary logistic regression (Enter) was used; (**b**) Binary logistic regression (backward) was used. **BMI**: body mass index; **CI**: confidence interval; **IL**: interleukin; **OSM**: Oncostatin M.

An Egyptian study in 2022 found that in patients who respond to anti-TNF therapy, OSM levels may decline slightly, but not to the same degree or persistence as other biomarkers (such as calprotectin or C-reactive protein), and persistent or elevated OSM levels after treatment often indicate persistent inflammation or a poor prognosis (Mohamed et al. 2022). Although OSM is a promising marker for IBD patient diagnosis and follow-up, its predictive performance for predicting the response to IBD treatment is limited (Mohamed et al. 2022; Saleh et al. 2024).

Results of multivariate logistic regression showed that OSM had a statistically significant effect (negative association) on reaching the ADL target TL. While the OR of 1.007 per pg/mL appears modest, this must be interpreted in the context of the observed biomarker range: each 1 pg/mL increase in OSM was associated with a 0.7% increase in the odds of failing to reach target trough levels. Given the median difference of 64 pg/mL between groups (134.61 vs. 198.61 pg/mL), this translates to clinically relevant risk stratification. The small effect size may limit the clinical utility of such a finding. However, this association may gain future clinical utility if it is incorporated into multi-parameter predictive models rather than used in isolation.

Results of serum 90K levels showed that there were no statistically significant differences between patients who reached the target TL of ADL and patients in remission compared to patients with IBD who did not reach the target TL and patients with active disease, respectively, despite a trend toward lower levels in TL non-achievers and in active disease. In a single-center observational cohort study of 48 patients with IBD (30 CD and 18 UC), patients who developed anti-infliximab antibodies and became non-responders had significantly higher baseline 90K serum levels compared to responder patients. This difference was significant in the total cohort and in CD, but not significant in UC (Pesole et al. 2023). Another study found that a group of patients with active CD had higher serum levels of 90K than healthy controls. This suggests that serum 90K may serve as an adjuvant biomarker for disease activity, even if it is not a specific marker for CD (Cibor et al. 2019). However, they did not study the correlation between serum 90K and the response to therapy, as their CD patients were receiving different therapies.

The current study's findings indicated that there were no significant differences in serum IL-12p40 levels between groups regarding target TL achievement or disease activity in patients with IBD. A cross-sectional study was conducted to assess biomarkers that predict lack of response to anti-TNF medication in moderate to severe UC patients and found that high IL12/23 p40 levels at week 2 could predict lack of response, indicating early inflammatory diversion toward the IL12/23 pathway and increased neutrophil recruitment, respectively, which account for the mechanistic failure of anti-TNF (Brandse et al. 2015). A prospective observational study conducted in Spain examined the relationship between anti-TNF drug levels and cytokine profiles, including IL-12, in 111 patients with CD treated with ADL and infliximab. It found that the ADL level was significantly associated with IL-12 ($p = 0.0252$) in univariable linear regression analyses, showing a weak negative relationship, that lost its significance in the multivariate analysis. The study noted that elevated IL-12 levels in patients requiring dose intensification could indicate either poor disease control necessitating higher doses or a direct effect of high ADL doses on cytokine regulation (Orts et al. 2021).

This study had some limitations, which should be noted. First, patients were collected from a single center in Iraq. Further research is needed to determine whether they accurately represent the overall number of patients with IBD in Iraq who are on ADL. Second, the sample size is relatively small, which may restrict the generalizability of the findings. Third, a fundamental limitation of this study is the cross-sectional design, which precludes establishing temporal relationships and causal inference. We cannot determine whether elevated serum OSM represents a baseline biological characteristic that predicts subsequent failure to achieve adalimumab trough levels, or whether OSM elevation is a consequence of inadequate drug exposure and persistent inflammatory activ-

ity. Fourth, the use of convenience sampling, while pragmatically necessary for this exploratory study, represents a significant methodological limitation that affects the interpretation of our biomarker findings. Convenience sampling from a tertiary referral center enriches for severe, refractory disease, inflating effect sizes and limiting generalizability to community-based IBD populations. To make reliable and accurate conclusions, the limitations of the study should be considered when interpreting the results, and future prospective regional cohorts should address these limitations before clinical implementation can be recommended.

Conclusion

Serum OSM levels were significantly higher in patients failing to achieve adalimumab target trough levels and were significantly associated with adalimumab TL achievement in this Iraqi cohort, demonstrating the feasibility of serum OSM measurement in a real-world clinical setting. These findings support further investigation of OSM as a pharmacokinetic biomarker in adalimumab drug monitoring.

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Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: Ethical approval was received from the University of Baghdad, College of Pharmacy ethical committee (reference number IDRECAUBCP742024k, date: 7 April 2024). The Iraqi Ministry of Health also gave its clearance.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

No use of AI was reported.

Funding

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Author contributions

Kadhim AM and Kadhim DJ Conceived and designed the study. Kadhim AM and Hussein RJ collected the data. Kadhim AM and Kadhim DJ prepared the draft manuscript. All authors have read and approved the final version of the manuscript.

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Data availability

All of the data that support the findings of this study are available in the main text.

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