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Serum IL-17A Protein as a Potential Diagnostic and Prognostic Biomarker in Iraqi Colorectal Cancer Patients

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ABSTRACT

Background: *Colorectal cancer (CRC) remains a primary global health concern and ranks as one of the leading causes of cancer-related deaths worldwide. In Iraq, the incidence of CRC has increased over recent years, particularly among adults over the age of 40. Inflammation is recognized as a key driver of CRC progression, with interleukin-17A (IL-17A) identified as a crucial pro-inflammatory cytokine involved in tumor growth, immune modulation, and metastasis.* ***Goal of study:*** *Our study aimed to evaluate the serum levels of IL-17A in Iraqi CRC patients and to assess its potential diagnostic and prognostic significance.* ***Material and Methods:*** *A case-control study involved 60 clinically diagnosed CRC patients and 60 healthy controls matched for age and sex. Serum samples were collected, separated by centrifugation, and stored at –40°C. IL-17A levels were measured using a sandwich ELISA kit.* ***Results:*** *Clinical data were recorded for correlation analysis, including tumor grade, stage, and patient demographics. Serum IL-17A levels were significantly elevated in CRC patients compared to healthy controls ($p<0.001$). Higher IL-17A concentrations were associated with advanced tumor stage and poor differentiation. ROC curve analysis indicated good diagnostic potential, with IL-17A as a promising non-invasive biomarker. Furthermore, elevated IL-17A levels were linked to poorer overall survival, suggesting prognostic relevance.* ***Conclusion:*** *Serum IL-17A levels may serve as a valuable diagnostic and prognostic biomarker in Iraqi colorectal cancer patients. Further large-scale studies are needed to validate its clinical utility in CRC detection and management.*

Keyword: CRC, IL-17A, Biomarker diagnosis.

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INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer-related mortality worldwide, accounting for over 1.9 million new cases and nearly 935,000 deaths annually (Sung et al., 2021). In Iraq, the burden of CRC has been increasing steadily, particularly among individuals aged 40 to 70 years, posing a significant public health challenge (Al-Azzawi et al., 2020). Despite advancements in treatment, CRC is often diagnosed at an advanced stage due to the lack of reliable non-invasive biomarkers for early detection and progression monitoring. Inflammation plays a critical role in the initiation and progression of colorectal cancer. Among pro-inflammatory cytokines, interleukin-17A (IL-17A), primarily secreted by Th17 cells, has attracted increasing attention for its dual role in tumor development. IL-17A contributes to tumorigenesis by promoting angiogenesis, enhancing tumor cell

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proliferation, and creating an immunosuppressive tumor microenvironment (Kryczek et al., 2009; Gaffen et al., 2014). Elevated levels of IL-17A have been observed in both tissue and serum samples of CRC patients and have been associated with tumor invasion, metastasis, and poor prognosis (Wu et al., 2020). Given its biological relevance, serum IL-17A has emerged as a promising non-invasive biomarker. Quantifying its levels may support early CRC detection, reflect disease activity, and assist in stratifying patients based on prognosis (Liu et al., 2021). However, limited data exist regarding its utility among Iraqi patients. This study assesses the diagnostic and prognostic significance of serum IL-17A protein levels in Iraqi colorectal cancer patients.

MATERIALS AND METHODS

Patients and Healthy Control Subjects

A case-control study was conducted between January 2024 and February 2025 involving 60 Iraqi patients clinically diagnosed with colorectal cancer by a subspecialist at the Najaf Alsharaf National Hospital for Oncology and Hematology Center. Clinical data were obtained from hospital records and patient case sheets. Patient parameters collected included age, gender, family history, and histopathological findings. Additionally, 60 age-matched healthy individuals (aged 40–70 years) were recruited as the control group.

Collection of Blood Samples

The total number of participants in this study was 120 individuals, divided into two groups: the first group included 60 patients diagnosed with CRC. In contrast, the second group comprised 60 healthy volunteers serving as controls. Blood samples were collected through venipuncture under aseptic conditions using a sterile syringe. Blood samples were obtained from colorectal cancer (CRC) patients and healthy controls, followed by centrifugation to separate the serum. The collected serum was stored at –40°C until further analysis. Serum IL-17A levels were quantified using a sandwich enzyme-linked immunosorbent assay (ELISA) kit. Human IL-17 is an enzyme used in an immunoassay for in vitro specific and quantitative determination of these cytokines in human serum. This test has been achieved according to the manufacturing company (Solarbio, China).

Calculation of results

Construct a standard curve by plotting the average OD for each standard on the vertical (Y) axis against the concentration on the horizontal (X) axis, and draw a best-fit curve through the points on the graph. These calculations can be best performed with computer-based curve-fitting software, and the best fit line can be determined by regression analysis, as demonstrated in **(Figure 1)**.

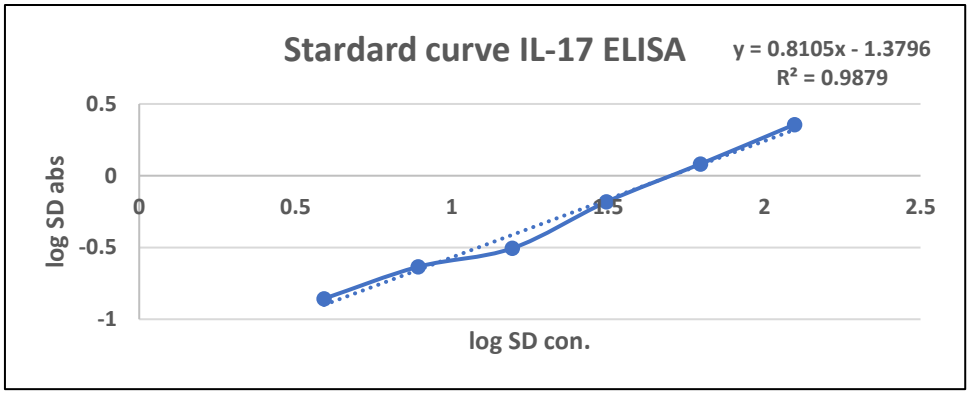

Figure 1: Standard curve of IL-17 concentration.

RESULT

Demographic Analysis

The mean age of colorectal cancer (CRC) patients was ~58.6 years (range 40–89), compared to ~55.9 years in the control group (40–89 years). This difference was not statistically significant (p ≈ 0.19). However, the age distribution showed notable shifts: 30% of CRC patients were aged 40–49, 28.3% were 50–59, and about 41.7% were ≥60 years old. By contrast, only 20% of controls were in their 40s, while a much larger fraction (63.3%) of controls were≥60. In other words, the control group skewed older (63% at least 60 years old, vs ~42% of patients ≥60; p ≈ 0.058). This suggests that a substantial subset of our CRC cases occurred in middle-aged adults (in their 40s and 50s), whereas the controls included more elderly individuals. as demonstrated in **(Table 2).**

Table 1: Demographic Analysis of CRC Patients and Controls.

	Patient (n=60)	Control (n=60)	P-value
Age (Years) **Mean ± SD**	**58.62 ± 12.3**	**55.93 ± 9.87**	**0.19**
Range	**40 – 89**	**40-89**	
40-49	**18 (30%)**	**12 (20)**	**0.058**
50-59	**17 (28.3%)**	**10 (16.7)**	
≥ 60	**25 (41.7)**	**38 (63.3)**	
Male	**36 (60 %)**	**34 (56.7)**	**0.43**
Female	**24 (40 %)**	**26 (43.3)**	

Expression of IL-17A serum level in Colorectal cancer

The result of **(Figure 2**) illustrate that serum IL-17A levels for patients with colorectal cancer (n =60) were compared to healthy control samples using ELISA. Represents an increase in IL-17A serum level: unpaired t-test, P value (****) ≤ 0.0001.

The Results indicated that ROC curve recorded IL-17A best performance characteristics, showing the highest sensitivity and specificity (96.6% and 91.6%, respectively) (AUC: 0.99 at a cut-off value of 7.92), as demonstrated in **(Table 2 and Figure 3).**

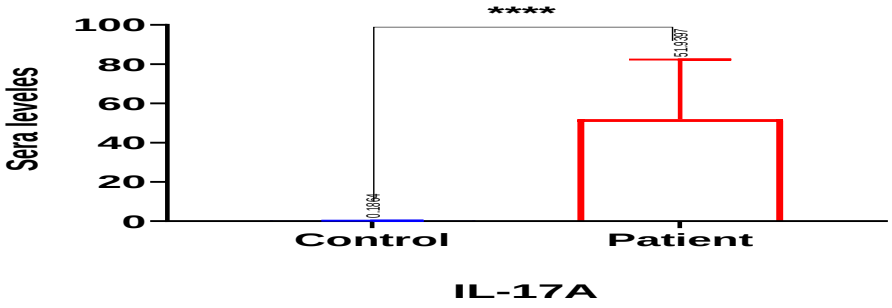

Figure (2). The serum IL-17A levels for patients with colorectal cancer.

Table 2: The ROC curve recorded of IL-17A.

Parameters	Cut off	AUC	95% CI	Explanation	Sensitivity%	Specificity%	P value significances
IL-17A (pg/ml)	< 7.92	0.990	0.9813 to 1.000	Excellent	96.6	91.6	<0.0001

AUC: area under the curve; CI; 95% confidence interval.

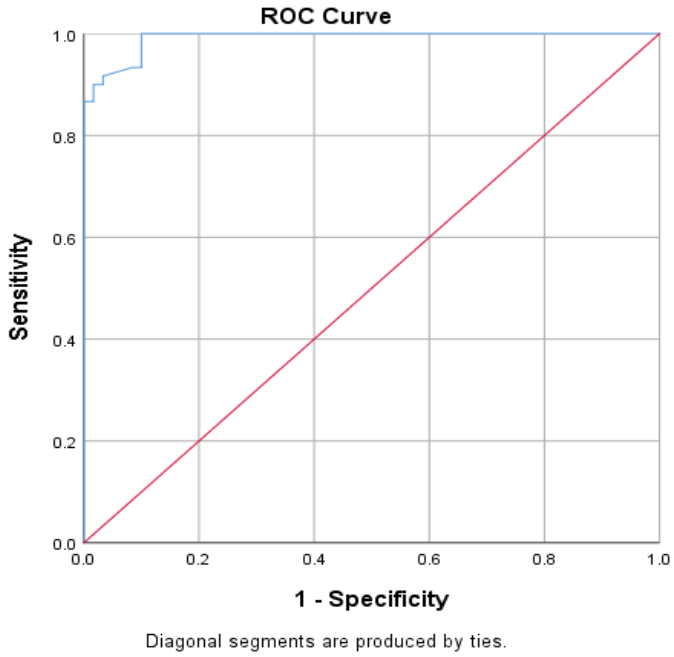

Figure (3): ROC curve analysis of IL-17A (pg/ml).

DISCUSSION

Several studies within Iraq report that CRC often presents in the fifth to seventh decades of life, but with a considerable minority of patients affected at younger ages. For example, a national study of 20,880 Iraqi CRC cases found that 31.8% were diagnosed before age 50 (early-onset CRC), with 68.2% at 50 or older (Ibrahem et al.,2022). Similarly, an observational study in Baghdad (2015–2021) reported a mean patient age of ~55 years and 31.6% of cases under 50 (Farhad et al.,2023).In the province of Karbala (2012–2020), the range of ages was 16 to 95, with a median age of 55. 139 patients (26.53%) were in the most common age group (61–70 years), followed by 108 patients (20.61%) in the 51–60 age group and 107 patients (20.42%) in the 41–50 age group (Mjali et al.,2024). In this study, the males were more dominant than the females, most of whom were from Najaf. However, no significant differences were identified regarding patients' sex and its association with CRC. This finding is supported by a study conducted by Ramadan et al. (2023), which indicates that in affluent Asian and Middle Eastern nations, there is a greater mortality-to-incidence ratio (MIR) for early-onset colorectal cancer (EO CRC) in females as opposed to males. Between 1990 and 2019, the female mortality-to-incidence ratio for early-onset colorectal cancer (EO CRC) was higher in 10 out of thirteen nations in these regions.

The role of serum IL-17A protein levels in colorectal cancer (CRC) is multifaceted, with evidence suggesting both diagnostic and prognostic implications. Elevated IL-17A levels have been associated with advanced disease stages and poorer outcomes, while also indicating potential protective effects in early tumor stages. A study measured serum levels of IL-17A protein in Colorectal cancer patients and healthy controls. The results indicated that IL-17A levels were higher in the cancer group, suggesting its potential as a biomarker for Colorectal cancer detection and progression. Serum IL-17A levels were found to be significantly higher in CRC patients compared to healthy controls, suggesting its potential as a diagnostic marker (Karabulut et al., 2016). A 2020 study of 125 CRC patients in blood noted that serum IL-17A protein was elevated in advanced-stage CRC (compared to early-stage). (Wang et al., 2020). Higher IL-17A mRNA levels correlate with better overall survival rates in early-stage CRC, indicating a protective role (Yang et al., 2022). Conversely, elevated serum IL-17A levels in advanced stages are linked to increased tumor progression and poor prognosis (Karabulut et al., 2016).

The previous study showed that IL-17 levels were significantly higher in patients with GC and CRC compared to the control group. Specifically, the serum IL-17 levels for the patient group were reported as 2.194 ± 0.03 pg/ml, while the control group had 1.462 ± 0.04 pg/ml. This difference was statistically significant ($p < 0.05$) (Rasheed et al., 2022). The Iraqi study (Rasheed & Al-Abassi) reported a modest ~1.5-fold increase in combined gastric/CRC patients (mean ~2.2 pg/mL) versus controls (1.46 pg/mL).

Sulaiman et al. (2022) measured IL-17A in the serum of 90 CRC patients (at diagnosis) and 30 healthy controls. They found elevated IL-17A in all CRC patient groups, with an ROC analysis yielding AUC ≈ 0.82. At an optimal cut-off of 67.18 pg/mL, IL-17A showed ~68% sensitivity and 85% specificity for diagnosing CRC. This indicates a good balance of sensitivity and specificity for serum IL-17A as a single marker in that cohort. Ma et al. (2022) evaluated serum IL-17A (along with other cytokines) in CRC patients. IL-17A alone showed an AUC = 0.88, with a very high sensitivity (~97%) but moderate specificity (~62%) in their population. (In this study, the cut-off was chosen to maximize sensitivity, hence the near-97% sensitivity but somewhat lower specificity.

The Romanian cohort (Tâlvan et al., 2024) observed much higher circulating IL-17A overall, with CRC patient sera averaging ~26 pg/mL versus ~7 pg/mL in healthy subjects—a ~3.7-fold change—using the same ELISA platform. This characteristic makes IL-17 a potential early indicator that something is going wrong in the colorectal area, particularly useful in clinical settings for early diagnosis. Early detection is essential because disease identification can improve treatment outcomes and survival rates. Elevated IL-17A mRNA/protein in tumors often associates with advanced stages, metastasis, and poorer prognosis in some studies.

CONCLUSION

The mean age of the CRC was 58.62 ± 12.3 years. Receiver operating characteristic (ROC) curve analysis indicated that IL-17A can be helpful as a predictive diagnostic marker for the early prediction of CRC in Iraqi patients.

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