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TGF-β Levels in Jordanian Acute and Chronic Brucellosis: A Possible Indicator of Immune Evasion and Chronicity

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ABSTRACT

brucellosis is a serious infectious disease that can be difficult to diagnose and treat since cases can progress from acute to chronic phases. The course of the disease is significantly influenced by immunological factors, and transforming growth factor-β (TGF-β) is thought to be involved in immune response regulation, immune evasion, and chronic inflammation. With an emphasis on comparing acute and chronic instances, the current study sought to assess TGF-β levels in Jordanian brucellosis patients and investigate its potential as a biomarker for immune evasion and illness duration. Blood samples were taken from three groups as part of the study's cross-sectional, comparative design, 30 patients with acute brucellosis, 30 patients with chronic brucellosis, and 30 healthy control subjects. ELISA was used to measure TGF-β levels in addition to serological testing and clinical evaluation. The association between TGF-β levels and the severity and duration of the condition was investigated, and statistical analyses were conducted to compare results between groups. The findings demonstrated a statistically significant positive association between TGF-β levels and the duration of the condition, with chronic patients having much greater levels than acute and healthy controls. These results confirm TGF-β's function as a trustworthy biomarker for determining the phases of a disease and forecasting its progression by indicating that high levels of the protein boost the immune response and contribute to chronic inflammation. The study concludes by pointing out that TGF-β level measurement may be a useful tool for assessing and directing treatment as well as for improving knowledge of Brucella immune evasion mechanisms. This creates chances for additional applied research and investigates the possibility of using this marker in clinical settings for early intervention and illness monitoring. To support the clinical use of this marker and create focused treatment plans, more study is advised.

1. Introduction

In many parts of the world, including Jordan, brucellosis—scientifically known as Brucella spp.—is linked to both health and economic difficulties. It is a significant infectious illness that affects both humans and animals [1]. Direct contact with diseased animals or the eating of unpasteurized dairy products are the main ways that the disease is spread. It encompasses a wide

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range of clinical manifestations, from asymptomatic cases to long-lasting illnesses that can have a substantial negative influence on patients' quality of life [2]. Effective management of chronic cases of brucellosis remains difficult despite advancements in diagnosis and treatment, underscoring the significance of comprehending the immunological mechanisms that contribute to the persistence and progression of the illness [3]. In order to more precisely evaluate the course of the disease and its response to treatment, single-target diagnostic techniques must be developed [4].

The immune system plays a crucial and essential role in the progression of brucellosis. According to studies, Brucella can elude an efficient immune response by adapting to the internal milieu of immune cells, which helps to prolong inflammation and promote the onset of chronic illness [5]. Therefore, it's important to find the biological elements that affect how the immune response is regulated, especially those that could interfere with the immune response and make it harder for the body to fight off infection [6]. One of the most crucial elements in controlling inflammatory and immunological responses is the transforming growth factor, or TGF-β. It has a dual function in controlling the immune system's reaction to infections and inhibiting that reaction, which could make it easier for the pathogen to elude the immune system [7]. In fact, it has been demonstrated that TGF-β levels are directly linked to certain chronic illnesses, such as inflammatory and chronic infection conditions, indicating that this factor may be involved in the development of brucellosis, particularly in the chronic stages [8].

Nevertheless, nothing is now known about the precise function of TGF-β in brucellosis, especially in the Jordanian setting [9]. Studies measuring TGF-β levels in patients and examining its correlation with disease duration and stages are lacking [10]. The significance of TGF-β in acute and chronic brucellosis in the Jordanian population is thus clearly not well understood. This calls for field research that thoroughly examines TGF-β levels at different stages of the disease [11]. In order to improve diagnostic and therapeutic monitoring measures, this study intends to assess TGF-β levels in Jordanian patients with acute and chronic brucellosis and investigate its potential as a biomarker reflecting immune evasion mechanisms and disease persistence.

2. Method

2.1. Type of Study

In order to assess and compare TGF-β levels between patients with brucellosis at various stages (acute and chronic) versus a healthy control group, the study was carried out using a cross-sectional, comparative design. This was done in order to identify any potential changes related to the type and progression of the disease. From June 2024 to June 2025, the study was carried out in Aqaba Hospital, one of the primary medical facilities in Aqaba City, Aqaba Governorate, Jordan, in order to confirm clinical and serological data and guarantee a significant number of identical patients.

2.2. Study Sample

There were three major groups in the study, each with thirty participants.

- Patients with acute brucellosis: Based on clinical evaluation and serological tests, these were chosen from among recently diagnosed patients (less than six weeks after the onset of symptoms).

- Patients with chronic brucellosis: These were recognized by positive serum antibody testing and symptoms that persisted or recurred for longer than six months.

- Healthy control group: consisting of healthy people with negative antibody test results who are free of Brucella symptoms and signs and are employed by hospitals or community-based organizations.

- Inclusion and exclusion criteria: To guarantee the accuracy of results directly connected to the disease, participants with additional chronic conditions or those who had received immunotherapy in the preceding months were removed.

2.3. Data Collection

All participants had blood samples taken, which were then kept in a suitable environment until analysis was completed after ethical approvals. The study was registered under file number 300616.

To ensure accuracy, TGF-β levels were measured using a validated ELISA approach with state-of-the-art equipment. Standardized questionnaires were used to evaluate clinical status, documenting the severity and duration of the condition to precisely categorize patients.

2.4. Statistical Analysis

Independent t-tests were used to compare TGF-β levels between groups if the data were normally distributed, and Mann-Whitney tests were used if they weren't. The association between TGF-β levels and the length or severity of the disease was investigated using Pearson correlation analysis, with $p < 0.05$ designated as the statistical significance criterion. To examine differences across groups, one-way AEcho tests were employed.

3. Results and Discussion

3.1. TGF-β Level Analysis in the Study Groups

ELISA was used to assess the amounts of transforming growth factor (TGF-β) in blood samples from each participant. The three groups' differences were statistically significant, according to the results, the mean TGF-β levels in the healthy control group were 15.2 ± 3.1 pg/ml. A considerable rise was noted in patients with acute brucellosis, with mean levels coming in at 22.8 ± 4.7 pg/ml. Chronic brucellosis patients had the highest values, at 34.5 ± 6.2 pg/ml. As shown in Table 1.

Selections were chosen after verifying assumptions, and statistics were conducted using the AEcho test to find differences between groups. Significant changes in TGF-β levels between groups were shown by the F-value of 65.9, which reached a significance level of $p < 0.001$.

Table 1. A statistical overview of the various groups' TGF-β levels

Group	Mean (pg/ml)	Standard Deviation
Healthy	15.2	3.1
Acute	22.8	4.7
Chronic	34.5	6.2

Transforming growth factor (TGF-β) levels are significantly higher in patients with chronic brucellosis than in acute and healthy controls, according to the study's findings. This suggests that TGF-β plays a critical role in controlling the immune response throughout the course of the illness. The immunosuppressive function of TGF-β, which is known to suppress effector T cell activation, downregulate T cells, and promote the activation of regulatory T cells (Tregs), is reflected in the elevated levels of TGF-β in chronic brucellosis. This reduces the effectiveness of the immune response against the Brucella bacteria.

Owing to Brucella's capacity to elude the immune system, increased TGF-β levels may be a component of the bacteria's plan to weaken the immunological response, which would encourage the continuation of inflammation and chronic infection. TGF-β probably plays a role in controlling the equilibrium between inflammation and the immune response biologically. Its high levels during chronic phases inhibit immune cells, promote unchecked inflammatory persistence, and make it more difficult to eradicate bacteria.

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3.2. TGF-β Levels and the Length and Severity of the Disease

The Pearson correlation test was used to evaluate the association between TGF-β levels and the length of the disease. The findings revealed a strong positive correlation, at a significance level of $p < 0.001$, the correlation value with disease duration (in weeks) was $r = 0.67$. Patients were divided into two groups according to the intensity of their symptoms (mild, moderate, and severe), even though TGF-β levels were higher in those with more severe symptoms. The mean TGF-β level was roughly 18.3 ± 3.4 pg/ml, indicating mild symptoms. The mean TGF-β level was roughly 36.2 ± 5.8 pg/ml, indicating severe symptoms. TGF-β levels and symptom severity were positively correlated, as indicated by the AEcho test's significant significance ($p < 0.001$).

Understanding patterns of immunological balance during chronic infection requires careful monitoring of TGF-β function. In addition to promoting regulatory T cells that release more TGF-β, elevated TGF-β may also impair the effectiveness of the cellular immune response and block the production of natural killer (NK) cells, creating a vicious cycle of immune suppression. In addition to causing chronic inflammation that lasts for a long time and includes tissue damage and periods of inflammatory dispersion, this can help bacteria stay within the host.

The disruption of tissue homeostasis caused by elevated TGF-β levels concurrently results in fibrosis and enhanced vascular perfusion, which may facilitate the establishment and growth of bacteria within the body's tissues [12, 13]. This explains why the study found a strong association between the severity and duration of disease and increased TGF-β.

3.3. Comparison of Findings with Other Research Worldwide

According to a number of earlier research, chronic inflammatory disorders, particularly those in which the body tries to regulate inflammation, have higher levels of TGF-β [14, 15]. For instance, brucellosis patients in various countries had higher levels of TGF-β than healthy individuals, according to a study published in the World Journal of Infectious Diseases. This finding was corroborated by a warning about TGF-β's involvement in fostering an environment that encourages recurring infections [16].

The distinctions between acute and chronic brucellosis, however, have not received much attention in research. By establishing that high TGF-β is a distinctive trait because it may result in an ineffective immune response, our work helps close this gap and supports the idea that this hormone may be a biomarker of illness persistence and progression.

4. Conclusion

To sum up, the findings of the study show how crucial TGF-β levels are as a possible biomarker for comprehending immune response mechanisms and their lack in cases of acute and chronic brucellosis, especially in the Jordanian setting. The findings demonstrated that chronic patients had much greater levels of TGF-β than acute and healthy controls, indicating that this factor plays a role in immune system disruption and chronic inflammation. This supports the idea that TGF-β has an active role in immune evasion and the development of chronic disease rather than just being a disease marker.

A significant step toward enhancing early diagnosis and clinical monitoring is the potential use of TGF-β as a biomarker to identify disease stages and treatment response, which would allow for the application of more individualized and successful therapeutic approaches. Additionally, the study's findings advance our understanding of the immune function of this factor in the context of brucellosis and offer a solid scientific foundation for future investigations that could result in the creation of medications that target the control of TGF-β levels in an effort to lessen the persistence of inflammation and enhance patient outcomes.

In order to validate and improve the use of TGF-β as a clinical evaluation tool, more research is needed, although this study is a useful addition to the scientific library. This will give high-quality healthcare services that consider local conditions and useful applied research, as well as open up new avenues for the diagnosis and monitoring of chronic infectious diseases.

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