

**Republic of Iraq  
Ministry of Higher Education  
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College of Dentistry**



# **Oral Findings, Oxidative Stress and Antioxidants Biomarkers in Serum and Saliva of Crohn's Patients In Relation To Treatment Modalities**

A Thesis

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# Abstract

**Background:**

Crohn's disease is an immunological disorder characterized by inflammation that can affect any part of the gastrointestinal tract. It is a chronic destructive condition that follows a relapsing-remitting course and associated with various intestinal and extraintestinal symptoms that can lead to disability and a poor quality of life.

Crohn's disease frequently presented with various oral manifestations as a consequence of inflammatory process of the disease, nutritional deficiency or medications side effects.

Several pharmacological agents including immunosuppressant and anti-tumor necrosis factor alpha antibodies that commonly utilized for targeting the pathological process of Crohn's disease by interruption with proinflammatory cytokines expression and inflammatory cell infiltration, leading to reduction of cellular oxidative stress status.

**Aims of the study:**

The objectives were to study the oral findings and to compare body mass index, oxidative stress (Malondialdehyde) and antioxidants (Glutathione and vitamin E) biomarkers in serum and saliva of Crohn's patients treated with Azathioprine monotherapy and compared with Azathioprine plus Infliximab combination therapy, then comparing both of them with that in the healthy control subjects.

**Subjects, Materials and Methods:**

Seventy- five subjects were incorporated in this study; fifty subjects presented with moderate to severe Crohn's disease that were divided into two subgroups, treated with different therapeutic modalities (Azathioprine monotherapy and anti -tumor necrosis factor alpha biological agent (Infliximab)

plus Azathioprine Combination therapy). While other twenty -five were age and gender matched healthy control subjects. Body mass index was determined by dividing the weight (kilogram) by square of height (square meter). Oral examination was done for each subject to detect the oral findings. Serum and saliva samples were collected from each subject enrolled in this study and salivary flow rate (ml\min) was measured for participants, then these samples were centrifuged and the supernatants were frozen for subsequent oxidative stress and antioxidants biomarkers assessments by using spectrophotometer and vitamin E ELISA kit.

**Results:**

The results showed that there was no significant difference ( $p>0.05$ ) found between the mean of body mass index of Crohn's patients and healthy control subjects. But the mean of body mass index was significantly reduced ( $p<0.05$ ) in Azathioprine monotherapy group than that in Combination therapy group.

Fungal infection was the main oral findings observed among 48% of Crohn's patients and it was more prevalent among those on combination therapy (60%) as comparing with those on Azathioprine monotherapy (36%).

Other oral findings that also noticed in Crohn's patients and according to their frequency from the highest to the lowest, were aphthous ulceration 26%, dysphagia 12%, hairy tongue 10%, atrophic glossitis 4%, lip swelling 4%, lichen planus and desquamative gingivitis 2% of patients.

Most of the oral findings were higher in Azathioprine monotherapy treated group than combination therapy treated group. Aphthous ulceration was the most prominent oral findings presented in 36% of patients in Azathioprine monotherapy group followed by dysphagia and hairy tongue in 16%, then atrophic glossitis and lip swelling in 8% and desquamative gingivitis in 4%, while oral findings in those on combination therapy were aphthous ulceration in 16%, dysphagia in 8%, hairy tongue and oral lichen planus in 4%.

The results showed that the mean of salivary flow rate in Crohn's patients was significantly lower ( $p < 0.001$ ) than that in healthy control subjects.

Mean of serum and saliva oxidative stress Malondialdehyde marker were significantly higher ( $p < 0.001$ ) in Crohn's patients than that of control subjects; however, the level of Malondialdehyde in Azathioprine monotherapy treated group was significant higher ( $p < 0.001$ ) than that of the combination therapy treated group.

Mean of Glutathione and vitamin E antioxidants biomarkers in serum and saliva of Crohn's patients were significantly lower ( $p < 0.001$ ) than that in control subjects; however, serum and saliva Glutathione and vitamin E levels in those on Azathioprine monotherapy were significantly lower ( $p < 0.001$ ) than those under combination therapy.

A significant positive linear correlation has been found between serum and saliva parameters (Malondialdehyde, Glutathione and vitamin E) in each Azathioprine and combination Crohn's groups.

The results showed that the correlation between the duration on combination therapy and oxidative stress biomarker (Malondialdehyde) was highly significant, negative linear correlation, while the correlations with antioxidants Glutathione and vitamin E markers were highly significant positive linear correlation.

On the other hand, the results showed that duration on Azathioprine monotherapy was significantly and positively correlated with serum and saliva Glutathione and serum vitamin E, while non-significant negative linear correlation was observed with serum and saliva Malondialdehyde.

### **Conclusions:**

This study shows an increase in oxidative stress and reduced antioxidant activity in Crohn's patients. Treatment with combination therapy has a superiority above Azathioprine monotherapy in controlling oxidative tissue damage and enhanced antioxidants system in Crohn's patients. Crohn's disease

associated with various oral findings as a result of inflammatory process and medication side effects. Fungal infection was the most prominent oral findings among Crohn's patients on combination therapy as a result of concomitant immunosuppressive effects that accounted for reduced immune response and increase the risk of opportunistic infections.