STUDIES ON SIGNIFICANCE OF COLONIC MUCUS CHANGES IN ULCERATIVE COLITIS

THESIS

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BY

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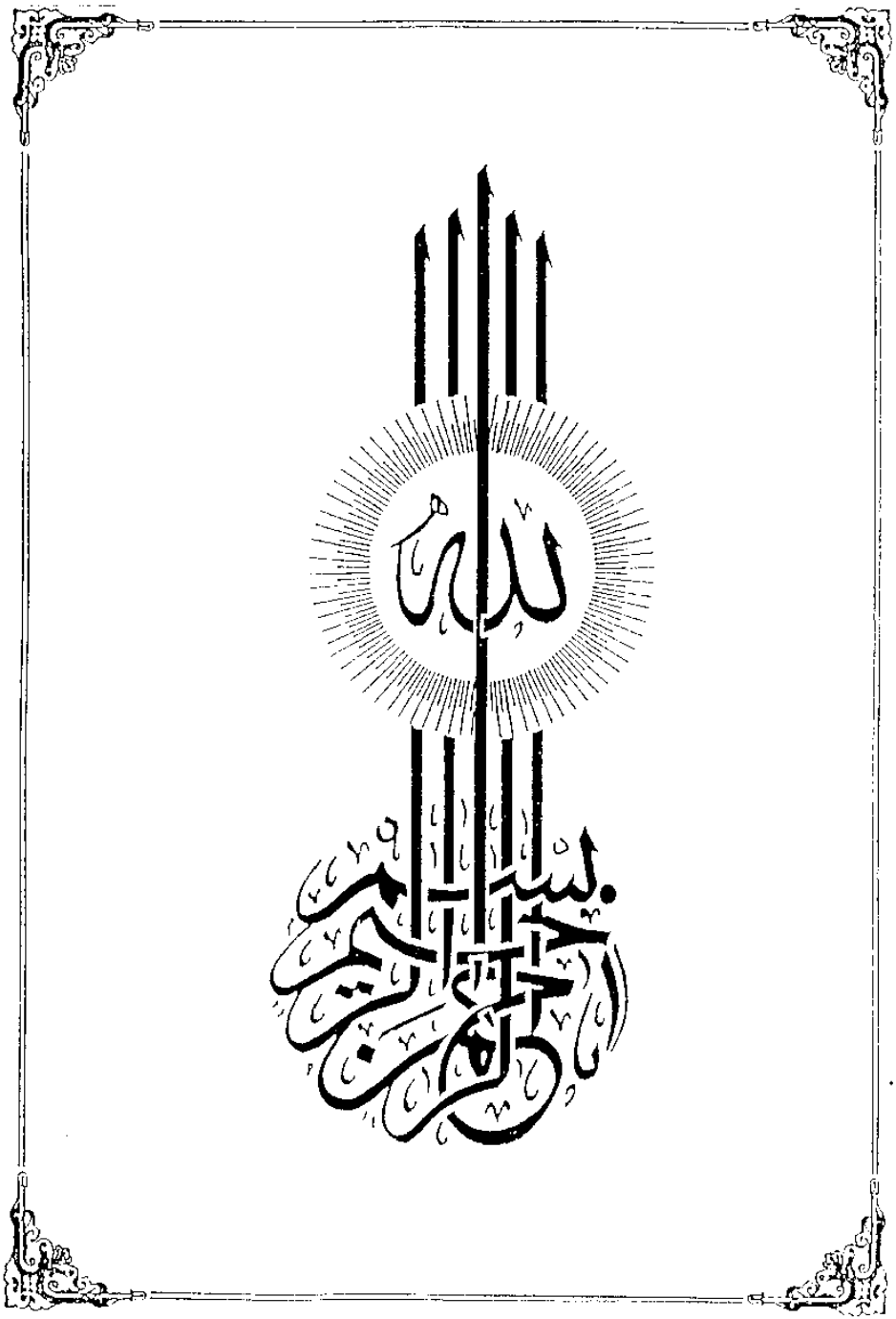

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ABSTRACT

In the left colon mucosal glycoproteins derived from goblet cells are highly sulphated. Depletion of goblet cell mucus is a striking histological feature of UC.

In the present study it was found that with increased disease duration there was an increased severity of the disease and increased liability to malignant changes.

The histologic findings of dysplasia were regarded as a marker for malignancy.

It was found also that there was neutral mucin depletion, but mucin depletion was more in acid mucin than neutral mucin which renders the colon more susceptible to enzymatic degradation by bacterial enzymes.

It was found also that acid mucin depletion was more in the active form of the disease.

One of the most important results of this study supported by many previous studies was that there was decreased mucin sulphation in patients with UC and colonic carcinoma and there was also depletion of carboxylated mucin but with less extent than sulphated mucin.

So, it is recommended that in cases of UC a follow up by sigmoidoscopic biopsy specimen and histopathological study is recommended to detect dysplasia and mucin changes early in order to detect malignant changes especially with long duration of the disease. In a conclusion mucin changes and its depletion is a good marker for malignancy in UC.

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INTRODUCTION

Mucus in the gastrointestinal tract adheres as a gel to surface epithelium producing an interface between lumen and mucosa.

Our important component of the normal colonic surface that serves to maintain its integrity is the dense layer of glycoprotein that coats the colonic surface (Daniel et al., 1983).

This coat appears to include both intrinsic colonc surface membrane-bound glycoproteins and high molecular weight mucin glycoproteins secreted by goblet cells.

Mucin glycoproteins are capable of forming a viscoelastic gel which in addition to lubricating the colonic surface to permit passage of luminal contents may play an important role in protecting the colonic epithelium from chemical and physical injury as well as resisting the invasion of patential pathogens.

Several reports indicate that alterations in mucin content may be associated with various diseases including inflammatory bowel disease (Filipe, M.I. et al., 1979).

However, despite the longstanding awareness that goblet cell mucin depletion is a frequent histologic hall-mark of ulcerative colitis (Filipe, M.I. et al., 1976). More detailed informations are limitted.

AIM OF THE STUDY

The aim of the present study is :

1. To study histopathological changes in ulcerative colitis.
2. To study the colonic mucus changes in ulcerative colitis patients.

MUCUS OF THE GASTROINTESTINAL TRACT

One of the important functions of the gastrointestinal epithelium is the secretion of mucus.

The major component of mucus is a high molecular weight glycoprotein (Mucin) which is responsible of the gel forming properties.

Mucin are giant glycoproteins (range 1-20 x 10^6 Da) which have linear protein core that is extensively glycosylated by O-linked oligosaccharide chains which account for over 80% of the dry weight.

The "bottle brush" arrangement of oligosaccharides around the protein core allows the mucin to bind large amounts of water, resulting in a gel that expands rapidly after secretion into the intestinal lumen.

This gel not only constitutes a physical barrier and lubricant but also generates a protective diffusion barrier for the underlying epithelium.

This effect is important in the stomach where the low pH also increases mucus viscosity at the luminal surface (Bhaskar et al. 1991).

Mucus also acts as a free radical scavenger, partly as a consequence of its ability to bind lipids (Gong et al. 1991).

Other mucus constituents include secretory immunoglobulin A (IgA), lysozyme, lactoferrine, α_1 antitrypsin, dialysable salts and N-glycosylated glycoproteins.

Growth factors are secreted in mucus for example: The secretion of both epidermal growth factor (EGF) and trefoil peptides by the specialized goblet cells found as an adaptive phenomenon adjacent to areas of ulceration (Wright et al. 1993).

Heat-stock protein is also secreted with mucus although its function is unknown (Winrow et al. 1993).

At least six different protein core sequences have been identified and these are differentially expressed in different tissues and in different disease states. These all have in common a high content of serine, threonine and proline and large numbers of Tandem repeat sequences.

Each mucin chain probably contains a few N-linked oligosaccharides but 150 or more 0-linked oligosaccharides (Strous et al. 1992).

These 0-linked chains are always initiated by N-acetylgalactosamine, α-linked into serine or threonine, but further extension of the oligosaccharide chain (up to 15or more carbohydrates) is characterized by enormous variation in