Comparative Histochemical Distribution of Mucins in Human Oropharynx During Development and Carcinogenesis

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Abstract

Background: Mucins are high-molecular-weight glycoproteins that play an essential role in protecting the mucosal surfaces of the upper aerodigestive tract. Their histochemical composition varies during fetal development, normal adult physiology, and malignant transformation, reflecting changes in epithelial differentiation and secretory function.

Objective: To compare the histochemical distribution of neutral mucins, sulphomucins, and sialomucins in the human oropharynx during fetal development, adulthood, and squamous cell carcinoma using conventional histochemical staining techniques.

Methods: This observational histochemical study included fetal, adult, and histopathologically confirmed squamous cell carcinoma specimens of the human oropharynx. Fifty fetal specimens were categorized into three gestational age groups (16–26 weeks, 27–32 weeks, and 33 weeks to full term), along with 30 normal adult specimens and 6 carcinoma specimens. Tissue sections were stained with Hematoxylin and Eosin (H&E), Periodic Acid–Schiff (PAS), PAS–Diastase, PAS–Phenyl Hydrazine, Alcian Blue (pH 2.5), Alcian Blue (pH 1.0), Aldehyde Fuchsin, Alcian Blue–PAS, and Aldehyde Fuchsin–Alcian Blue to identify neutral mucins, sulphomucins, and sialomucins.

Results: All three mucin types were detected throughout fetal development, although their distribution varied with gestational age. Early fetal specimens predominantly demonstrated neutral mucins and sulphomucins, whereas progressive gestation showed a relative increase in sialomucins. Adult oropharyngeal tissues demonstrated abundant neutral mucins with predominance of sulphomucins among acidic mucins. In squamous cell carcinoma specimens, acidic mucins predominated, with a marked increase in sialomucin expression and a corresponding reduction in neutral mucins and sulphomucins.

Conclusion: Histochemical alterations in mucin composition occur during normal development and become more pronounced during malignant transformation. The predominance of sialomucins in squamous cell carcinoma suggests their potential role as indicators of epithelial dedifferentiation and carcinogenesis. Histochemical evaluation of mucins may therefore provide useful adjunctive information for understanding tumor biology and disease progression.

Keywords: Oropharynx; Mucins; Histochemistry; Sialomucin; Sulphomucin; Squamous Cell Carcinoma.

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Introduction

The oropharynx is an important anatomical region of the upper aerodigestive tract that serves as a common pathway for respiration, deglutition, and phonation. It extends from the soft palate superiorly to the upper border of the epiglottis inferiorly and includes the base of the tongue, palatine tonsils, soft palate, and posterior pharyngeal wall. The mucosal lining of the oropharynx consists predominantly of stratified squamous non-keratinized epithelium supported by numerous minor salivary glands that secrete mucins essential for maintaining epithelial hydration, lubrication, and protection against mechanical trauma, microbial invasion, and chemical irritation. Normal structural development and physiological function of the oropharyngeal mucosa depend on the appropriate synthesis and secretion of these glycoproteins. (1), (2)

Mucins are high-molecular-weight glycoproteins synthesized by epithelial cells and submucosal glands. Their carbohydrate-rich side chains confer viscoelastic properties that facilitate lubrication while simultaneously forming a protective barrier against pathogens and environmental insults. Besides their mechanical protective function, mucins regulate epithelial differentiation, cell signaling, immune defense, and tissue homeostasis. Alterations in mucin composition are closely associated with developmental maturation and several pathological conditions, including chronic inflammation, epithelial dysplasia, and malignant transformation. (3), (4)

Histochemically, epithelial mucins are broadly classified into neutral mucins and acidic mucins, the latter comprising sulphomucins and sialomucins. Neutral mucins are mainly responsible for lubrication and epithelial protection, whereas acidic mucins contribute to antimicrobial defense, maintenance of surface hydration, and regulation of ionic balance. Sulphomucins contain sulphate groups that provide resistance to enzymatic degradation, while sialomucins contain terminal sialic acid residues involved in cell adhesion, epithelial differentiation, and modulation of immune responses. The relative proportions of these mucins vary according to anatomical site, developmental stage, and pathological condition, making histochemical evaluation valuable for understanding tissue maturation and disease progression. (5), (6)

During fetal development, the epithelial lining and submucosal glands of the oropharynx undergo continuous differentiation accompanied by progressive changes in mucin synthesis. Early gestational stages are characterized predominantly by neutral mucins and sulphomucins, whereas advancing gestation is associated with increasing expression of sialomucins, reflecting maturation of secretory function and epithelial differentiation. These developmental changes are believed to represent physiological adaptation required for postnatal airway protection and normal glandular function. Evaluation of mucin distribution during fetal life therefore provides important insights into the biological maturation of the upper aerodigestive tract. (3), (5)

In malignant transformation, epithelial cells undergo profound biochemical and structural alterations that are frequently accompanied by changes in glycoprotein synthesis. Neoplastic cells often exhibit altered glycosylation patterns resulting in increased production of acidic mucins, particularly sialomucins, together with reduction or redistribution of neutral mucins and sulphomucins. Such alterations are considered consequences of abnormal glycosyltransferase activity, altered cellular differentiation, and deregulated mucin gene expression. These histochemical changes may precede obvious morphological abnormalities and therefore have potential diagnostic and prognostic significance in epithelial malignancies. (4), (7)

A variety of histochemical staining techniques have been developed to identify different classes of mucins. Periodic Acid–Schiff (PAS) staining demonstrates neutral mucins, whereas Alcian Blue at different pH levels identifies acidic mucins. Aldehyde Fuchsin specifically demonstrates sulphated mucins, while combined staining methods such as Alcian Blue–PAS and Aldehyde Fuchsin–Alcian Blue enable simultaneous differentiation of neutral mucins, sulphomucins, and sialomucins within the same tissue section. These techniques remain reliable, cost-effective, and widely accepted methods for studying epithelial mucin distribution in both developmental biology and surgical pathology. (6), (7), (8)

Although several studies have investigated mucin histochemistry in different regions of the respiratory and gastrointestinal tracts, comparatively fewer studies have specifically evaluated the developmental and carcinogenic changes occurring in the human oropharynx. Understanding these alterations may improve knowledge of epithelial maturation and provide useful histopathological markers of malignant transformation. Therefore, the present study was undertaken to compare the histochemical distribution of neutral mucins, sulphomucins, and sialomucins in the human oropharynx during fetal development, normal adult life, and squamous cell carcinoma using conventional histochemical staining techniques.

Materials and Methods

Study Design and Setting

This observational, descriptive histochemical study was conducted in the Department of Anatomy using archived fetal, adult, and histopathologically confirmed carcinoma specimens of the human oropharynx. The study was designed to compare the histochemical distribution of epithelial mucins during normal fetal development, adult life, and malignant transformation.

Study Specimens

The study included a total of **86 human oropharyngeal specimens**, comprising:

- **50 fetal specimens**
- **30 normal adult specimens**
- **6 histopathologically confirmed squamous cell carcinoma specimens**

The fetal specimens were categorized according to gestational age into three groups:

- Group I: 16–26 weeks of gestation
- Group II: 27–32 weeks of gestation
- Group III: 33 weeks to full term

Adult specimens were collected from normal oropharyngeal tissues without evidence of inflammatory or neoplastic pathology. Carcinoma specimens consisted of histopathologically confirmed squamous cell carcinoma of the oropharynx.

Inclusion Criteria

- Human fetal oropharyngeal specimens with gestational age between 16 weeks and full term.
- Histologically normal adult oropharyngeal tissue.
- Histopathologically confirmed squamous cell carcinoma specimens of the oropharynx.

Exclusion Criteria

- Poorly preserved tissue specimens.
- Autolyzed fetal tissues.
- Specimens with inadequate tissue for histochemical evaluation.
- Adult tissues showing inflammatory or degenerative changes.

Tissue Processing

Immediately after procurement, tissue specimens were fixed in 10% neutral buffered formalin. Following fixation, tissues were processed by conventional paraffin-embedding techniques. Serial sections of approximately 4–5 µm thickness were prepared using a rotary microtome and mounted on clean glass slides for routine histological and histochemical staining.

Histochemical Staining

All tissue sections were subjected to Hematoxylin and Eosin (H&E) staining for assessment of general histological architecture. Histochemical demonstration of mucins was performed using the following staining methods:

- Periodic Acid–Schiff (PAS)
- PAS–Diastase (PAS-D)
- PAS–Phenyl Hydrazine (PAS-PH)
- Alcian Blue (pH 2.5)
- Alcian Blue (pH 1.0)
- Aldehyde Fuchsin (AF)
- Alcian Blue–PAS (AB-PAS)
- Aldehyde Fuchsin–Alcian Blue (AF-AB)

These staining techniques enabled differentiation of neutral mucins, sulphomucins, and sialomucins based on their characteristic histochemical reactions.

Histochemical Evaluation

The stained sections were examined independently under a light microscope at appropriate magnifications. Histological features of the surface epithelium and glandular tissue were evaluated using H&E staining. Histochemical assessment focused on the localization and relative intensity of neutral mucins, sulphomucins, and sialomucins within the epithelial and glandular components of the oropharynx.

The staining intensity was graded semi-quantitatively as:

- (+) Mild
- (++) Moderate
- (+++) Strong

Particular attention was given to changes in mucin composition across different gestational age groups, normal adult tissues, and carcinoma specimens.

Outcome Measures

The primary outcome measure was the comparative distribution of:

- Neutral mucins
- Sulphomucins
- Sialomucins

among fetal, adult, and squamous cell carcinoma specimens of the human oropharynx.

Secondary observations included changes in epithelial differentiation, glandular architecture, and alterations in mucin composition associated with fetal maturation and malignant transformation.

Results

A total of 86 human oropharyngeal specimens were examined histochemically, including 50 fetal specimens, 30 normal adult specimens, and 6 histopathologically confirmed squamous cell carcinoma specimens. Fetal specimens were categorized into three gestational age groups: 16–26 weeks, 27–32 weeks, and 33 weeks to full term. Histochemical evaluation demonstrated the presence of neutral mucins, sulphomucins, and sialomucins in all groups; however, their relative distribution varied according to developmental stage and malignant transformation.

Table 1. Histochemical distribution of mucins during fetal development of the human oropharynx

Gestational group	Neutral mucins	Sulphomucins	Sialomucins	Predominant finding
16–26 weeks	High	High	Low	Neutral mucins with sulphomucin predominance

27–32 weeks	High	Moderate	Moderate	Balanced sulpho- and sialomucins
33 weeks –term	High	Low	High	Progressive increase in sialomucins

During fetal development, all three mucin types were identified in the glandular tissue of the oropharynx. The earliest gestational group (16–26 weeks) demonstrated abundant neutral mucins together with predominance of sulphomucins among acidic mucins. Between 27 and 32 weeks, the proportion of sialomucins increased while sulphomucins gradually declined. Near term (33 weeks to full term), sialomucins became the predominant acidic mucin, indicating progressive maturation of epithelial secretory function.

Table 2. Comparison of mucin distribution between fetal and adult oropharynx

Group	Neutral mucins	Sulphomucins	Sialomucins
Fetal (16–26 weeks)	High	High	Low
Fetal (27–32 weeks)	High	Moderate	Moderate
Fetal (33 weeks –term)	High	Low	High
Adult	Very High	High	Low

Comparison between fetal and adult tissues showed that neutral mucins remained abundant throughout development. However, acidic mucins exhibited characteristic developmental changes, with sulphomucins predominating during early fetal life and sialomucins increasing toward term. Adult tissues showed restoration of sulphomucin predominance together with abundant neutral mucins, representing the normal histochemical pattern of the mature oropharynx.

Table 3. Histochemical characteristics of normal adult oropharyngeal tissue

Histological feature	Observation
Surface epithelium	Stratified squamous non-keratinized epithelium
Glandular tissue	Well-developed mucous glands
Neutral mucins	Predominant
Acidic mucins	Present
Predominant acidic mucin	Sulphomucin

Histological examination of adult specimens demonstrated stratified squamous non-keratinized epithelium with well-developed submucosal glands. Histochemically, neutral mucins were the predominant secretory product. Among acidic mucins, sulphomucins were more abundant than sialomucins, indicating the normal mature secretory phenotype of adult oropharyngeal glands.

Table 4. Histochemical distribution of mucins in squamous cell carcinoma of the oropharynx

Histological feature	Observation
Number of specimens	6
Epithelial morphology	Proliferated stratified squamous epithelium
Neutral mucins	Minimal
Acidic mucins	Markedly increased
Predominant acidic mucin	Sialomucin

Histopathological examination of carcinoma specimens revealed proliferated stratified squamous epithelium with increased glandular activity. Neutral mucins were markedly reduced, whereas acidic mucins predominated. Sialomucins showed the strongest histochemical reaction, while sulphomucins were comparatively decreased, demonstrating a characteristic alteration in mucin composition associated with malignant transformation.

Table 5. Overall comparison of mucin distribution during development and carcinogenesis

Tissue group	Neutral mucins	Sulphomucins	Sialomucins
Early fetus	High	High	Low
Late fetus	High	Low	High
Adult	Very High	High	Low
Squamous cell	Low	Low	Very High

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Overall, the histochemical pattern demonstrated a gradual transition from sulphomucin predominance during early fetal development to increasing sialomucin expression near term. Adult tissues exhibited abundant neutral mucins together with predominance of sulphomucins among acidic mucins. In contrast, squamous cell carcinoma showed a marked shift toward sialomucin predominance accompanied by depletion of neutral mucins, suggesting that alterations in mucin composition are associated with epithelial dedifferentiation and carcinogenesis.

Discussion

The present study compared the histochemical distribution of epithelial mucins in the human oropharynx during fetal development, normal adulthood, and squamous cell carcinoma. Histochemical analysis demonstrated that all three major mucin types—neutral mucins, sulphomucins, and sialomucins—were present throughout development; however, their relative proportions varied according to developmental stage and malignant transformation. The most notable finding was the progressive increase in sialomucin expression with advancing gestation and its marked predominance in squamous cell carcinoma, suggesting that alterations in mucin composition accompany both epithelial maturation and carcinogenesis.

The fetal oropharynx demonstrated characteristic developmental changes in mucin composition. Early gestational specimens (16–26 weeks) contained abundant neutral mucins together with predominance of sulphomucins among acidic mucins. As gestation progressed, sulphomucins gradually decreased while sialomucins increased, becoming the predominant acidic mucin near term. These findings indicate progressive maturation of secretory epithelial cells and modification of glycoprotein synthesis during fetal development. Similar developmental alterations in epithelial mucins have been reported in previous histochemical studies, which demonstrated that mucin composition changes according to epithelial differentiation and maturation during fetal life. These observations support the concept that mucin expression reflects developmental regulation of glycosyltransferase activity and secretory cell differentiation. (9), (10)

Adult oropharyngeal tissues exhibited abundant neutral mucins together with predominance of sulphomucins over sialomucins among acidic mucins. Neutral mucins contribute to lubrication and maintenance of epithelial integrity, whereas sulphomucins provide resistance to enzymatic degradation and protect the mucosal surface against chemical and microbial injury. This predominance of sulphomucins in normal adult tissues is consistent with the physiological protective role of mature respiratory and oropharyngeal mucosa. Similar histochemical findings have been described using Alcian Blue, PAS, and Aldehyde Fuchsin staining techniques, demonstrating that normal adult respiratory epithelium contains abundant neutral mucins with sulphomucin-rich acidic secretions. (10), (11)

The most significant alteration observed in the present study occurred in squamous cell carcinoma of the oropharynx. Carcinoma specimens demonstrated a marked reduction in neutral mucins together with predominance of acidic mucins, particularly sialomucins. This shift from sulphomucin-rich secretions in normal tissues to sialomucin-rich secretions in malignant tissues probably reflects abnormal glycoprotein biosynthesis resulting from altered glycosyltransferase activity during neoplastic transformation. Increased expression of sialomucins has been associated with loss of normal epithelial differentiation, increased cellular proliferation, altered adhesion, and enhanced invasive potential. Previous investigators similarly reported that malignant epithelial tissues exhibit increased sialomucin production accompanied by reduction of neutral mucins, supporting the usefulness of mucin histochemistry in identifying biochemical alterations associated with carcinogenesis. (12), (13)

Altered mucin composition during malignant transformation has important biological implications. Sialic acid-rich glycoproteins influence cell-to-cell adhesion, cellular recognition, immune evasion, and interactions between tumor cells and the extracellular matrix. Increased sialomucin expression may therefore facilitate tumor progression by reducing intercellular cohesion and promoting invasion of adjacent tissues. Conversely, reduction of neutral mucins may diminish the protective epithelial barrier, increasing susceptibility to chronic irritation and neoplastic progression. These observations support the hypothesis that histochemical alterations in mucins represent early biochemical events occurring before obvious structural abnormalities become apparent. Similar conclusions have been reported in studies evaluating mucin alterations in gastrointestinal and respiratory tract malignancies. (12), (14), (15)

The present findings further emphasize the diagnostic value of conventional histochemical techniques. Combined staining methods, including PAS, Alcian Blue, Alcian Blue–PAS, and Aldehyde Fuchsin–Alcian Blue, effectively differentiated neutral mucins, sulphomucins, and sialomucins within the same tissue sections. Although immunohistochemistry and molecular techniques provide greater specificity, conventional histochemistry remains inexpensive, reproducible, and readily available in routine pathology

laboratories, particularly in resource-limited settings. Histochemical evaluation of mucin distribution therefore continues to serve as a valuable adjunct in studying epithelial differentiation and pathological alterations.

A major strength of the present study is the direct comparison of fetal, adult, and carcinoma specimens using identical histochemical methods, allowing evaluation of developmental and pathological changes within the same anatomical site. However, certain limitations should be acknowledged. The carcinoma group included a relatively small number of specimens, and only squamous cell carcinoma was evaluated. Furthermore, the study relied exclusively on histochemical methods without molecular characterization of individual mucin genes or glycoproteins. Future studies involving larger sample sizes, different histological grades of carcinoma, and immunohistochemical or molecular analysis of mucin expression would provide additional insight into the biological significance of these alterations.

Overall, the present study demonstrates that epithelial mucins undergo predictable developmental modifications during fetal maturation and significant alterations during malignant transformation. The progressive increase in sialomucins from late fetal life to carcinoma, together with the reduction of neutral mucins and sulphomucins in malignant tissues, supports the concept that mucin histochemistry reflects changes in epithelial differentiation and may serve as a useful adjunct in the evaluation of carcinogenesis. These findings contribute to a better understanding of the histobiology of the human oropharynx and provide a basis for future investigations exploring the prognostic and diagnostic significance of mucin expression in head and neck malignancies.

Conclusion

The present study demonstrated that the histochemical distribution of epithelial mucins in the human oropharynx undergoes distinct changes during fetal development, adulthood, and malignant transformation. Neutral mucins, sulphomucins, and sialomucins were identified in all study groups; however, their relative distribution varied according to the stage of epithelial differentiation. Early fetal specimens predominantly exhibited neutral mucins and sulphomucins, whereas advancing gestation was associated with a progressive increase in sialomucin expression. In normal adult tissues, neutral mucins remained abundant with sulphomucins representing the predominant acidic mucin, reflecting the normal protective function of the mature oropharyngeal mucosa.

Squamous cell carcinoma specimens demonstrated a marked alteration in mucin composition characterized by increased acidic mucins, particularly sialomucins, together with a reduction in neutral mucins and sulphomucins. These findings suggest that changes in mucin histochemistry are closely associated with epithelial dedifferentiation and malignant transformation. Conventional histochemical staining techniques remain reliable and cost-effective methods for evaluating mucin composition and may serve as useful adjuncts in understanding epithelial maturation, diagnosing pathological alterations, and providing insight into the biological behavior of oropharyngeal squamous cell carcinoma.

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