



Received: 18 Aug 2026

Revised: 06 Sep 2026

Accepted: 27 Sep 2026

Published: 16 Oct 2026

2026: OCTOBER - IJMSDH

Page No - 57-70

DOI - 10.55640/ijmsdh-spc-09

Article Citation: Mahkamov Nosirjon Joraevich, & Muratov Fayoziddin Baxodirovich. (2026). Morphological and Immunohistochemical Features of The Gastric Mucosa in Metabolic Syndrome. International Journal of Medical Science and Dental Health, 1(01), 57-70. <https://doi.org/10.55640/ijmsdh-spc-09>

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Morphological and Immunohistochemical Features of The Gastric Mucosa in Metabolic Syndrome

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Abstract

This study examined morphological, morphometric, and immunohistochemical changes in the gastric mucosa in patients with metabolic syndrome. Gastric tissue samples from 83 patients with confirmed metabolic syndrome were analyzed, including 27 men and 56 women. The control group included 18 samples. Histological and morphometric examinations were performed, and the expression of iNOS and CAIX was also evaluated. The results showed that metabolic syndrome was associated with inflammation, impaired microcirculation, glandular atrophy, stromal fibrosis, and dystrophic changes in the gastric epithelium. In men, atrophic and sclerotic changes developed earlier, while in women these changes became more pronounced at the age of 45-59 years. Increased expression of iNOS and CAIX in this age group reflected stronger hypoxic and oxidative stress in the gastric mucosa. The findings suggest that age and sex should be considered when assessing gastric mucosal changes in patients with metabolic syndrome.

Keywords: Metabolic syndrome, gastric mucosa, atrophy, fibrosis, morphometry, iNOS, CAIX, immunohistochemistry.

1. Introduction

Metabolic syndrome is one of the most common metabolic disorders today. It is usually associated with abdominal



obesity, insulin resistance, arterial hypertension, and abnormal lipid metabolism. These changes affect several organs and systems at the same time. Recent global analyses show that the prevalence of metabolic syndrome has increased markedly since 2000. By 2023, it was reported in about 31.0% of women and 25.7% of men, affecting an estimated 1.54 billion adults worldwide [1, 2].

The effects of metabolic syndrome are not limited to the cardiovascular and endocrine systems. Insulin resistance, hyperglycemia, dyslipidemia, and chronic low-grade inflammation may also influence the gastrointestinal tract. Large prospective studies have shown that metabolic syndrome and some of its components are associated with a higher risk of gastrointestinal cancers [2, 3, 17].

Chronic inflammation of the gastric mucosa is also common in patients with obesity and metabolic disorders. Histological studies of gastric specimens obtained during bariatric surgery have reported active and inactive chronic gastritis, lymphoid follicles, mucosal atrophy, and intestinal metaplasia. Some studies have also found an association between body mass index, age, and the presence of intestinal metaplasia. These findings show that obesity is linked not only with functional disturbances but also with structural changes in the gastric mucosa [6, 7, 8].

Helicobacter pylori infection may further influence these changes. Recent systematic reviews and meta-analyses have shown an association between *H. pylori* infection, metabolic syndrome, and insulin resistance. Chronic inflammation caused by the infection may worsen metabolic disturbances, while metabolic syndrome may create conditions for persistent inflammation. For this reason, morphological assessment of the gastric mucosa is especially important when metabolic syndrome and *H. pylori* infection are present together [4, 5, 7].

Obesity is also associated with changes in local immune activity in the stomach. A recent immunohistochemical study showed an increased number of macrophages, mast cells, and newly formed microvessels in the gastric mucosa of patients with obesity. Some of these changes were associated with body mass index. This suggests that local inflammation and angiogenesis are active processes in the gastric mucosa in obesity [8, 9].

The stomach is not only a digestive organ but also an endocrine organ that produces biologically active substances. Recent immunohistochemical studies have examined ghrelin-producing cells in different areas of the stomach in patients with obesity. Their number and activity may vary depending on sex,

type 2 diabetes, hypertension, and other metabolic conditions. These findings support the need to study gastric mucosal changes not only by routine histology but also by immunohistochemical methods [10, 11, 12, 13].

The possible relationship between metabolic syndrome and precancerous gastric changes is also important. In patients with gastric intestinal metaplasia and metabolic syndrome, increased VEGF levels have been reported, while higher leptin levels were mainly associated with metabolic syndrome. These findings suggest a possible link between metabolic disturbances, chronic inflammation, angiogenesis, and tissue remodeling in the gastric mucosa [3, 9, 16].

Chronic atrophic gastritis and intestinal metaplasia are important morphological conditions that may precede gastric adenocarcinoma. Therefore, current gastroenterology guidelines give special attention to proper biopsy sampling, assessment of mucosal atrophy and metaplasia, and follow-up of patients at increased risk. These approaches help identify patients who may need closer endoscopic and morphological surveillance [14, 15, 16].

The OLGA and OLGIM staging systems are particularly useful for this purpose. A recent meta-analysis of prospective studies showed that OLGA stages III-IV are associated with a markedly increased risk of gastric cancer. A similar increase in risk was found in patients with advanced OLGIM stages. Therefore, accurate morphological assessment of atrophy and intestinal metaplasia is important not only for diagnosis but also for risk stratification [14, 18].

Gastric cancer remains an important global health problem. According to GLOBOCAN 2022, gastric cancer accounted for about 4.9% of all newly diagnosed cancers and 6.8% of cancer-related deaths worldwide. Recent epidemiological studies also indicate that overweight and obesity, particularly abdominal obesity, may be associated with a higher risk of gastric cardia cancer [3, 17].

Thus, in metabolic syndrome, inflammation, impaired microcirculation, epithelial and glandular atrophy, stromal remodeling, and metaplastic changes may develop together in the gastric mucosa. However, the age- and sex-related features of these changes, especially their relationship with hypoxia and oxidative stress markers, are still not fully understood. Therefore, combined morphological, morphometric, and immunohistochemical assessment of the gastric mucosa in metabolic syndrome is important for identifying early structural changes and defining high-risk patient groups [6, 8, 12, 18].



Aim of the study: to evaluate morphological, morphometric, and immunohistochemical changes in the gastric mucosa in metabolic syndrome, with attention to age and sex differences, and to determine their value for early diagnosis.

2. Methods

The study included gastric tissue samples from 83 patients with confirmed metabolic syndrome. Among them, 27 were men and 56 were women. The patients were divided into age and sex groups, with particular attention to men and women aged 18–44 and 45–59 years. The control group included 18 gastric tissue samples from individuals who died from causes unrelated to gastric disease.

The tissue samples were fixed in 10% neutral buffered formalin and processed by standard histological methods. Paraffin blocks were prepared, and sections 4–5 μm thick were obtained. The sections were stained with hematoxylin and eosin, PAS reaction, and Van Gieson stain. The gastric mucosa was evaluated for epithelial changes, glandular atrophy, stromal fibrosis, vascular changes, and inflammatory cell infiltration.

Morphometric examination was performed using a NanoZoomer digital slide scanner. Digital images were analyzed with QuPath and ImageJ software. The main parameters included total mucosal thickness, volume density of fundic glands, epithelial height, thickness of the lamina propria, stromal area between the glands, capillary wall thickness, lymphocytic infiltration, and epithelial apoptosis.

Immunohistochemical examination was used to assess changes related to hypoxia and oxidative stress in the gastric mucosa. The expression of iNOS and CAIX was studied. The

intensity of immunostaining was evaluated using the REMMELE and STEGNER scoring system from 0 to 3 points. The expression of these markers was compared between age and sex groups.

3. Results

Microscopic examination of the gastric mucosa in men with metabolic syndrome showed that the changes were different depending on age. Clear differences were seen between men aged 18–44 years and those aged 45–59 years. These differences involved the surface epithelium, gastric glands, stroma, and small blood vessels.

In men aged 18–44 years, the general structure of the gastric mucosa was mostly preserved. However, mild dystrophic changes were seen in the surface epithelial cells. In some areas, vacuolization and slight desquamation of the epithelium were present. The lamina propria showed small areas of lymphocytic and plasma cell infiltration. Mild tissue edema and uneven blood filling of small vessels were also noted.

The fundic glands were generally preserved in this age group. Still, in some samples, the secretory cells in the upper parts of the glands were smaller than normal. Mild dystrophic changes were also found in parietal and chief cells. Inflammatory cells were more common in the stroma between the glands. Some areas showed dilated capillaries and mild perivascular edema.

Overall, the changes in men aged 18–44 years were mainly similar to superficial active gastritis. Severe destruction of the epithelium and widespread glandular atrophy were uncommon. Therefore, the gastric changes in this age group can mainly be described as early dystrophic, inflammatory, and microcirculatory disturbances.

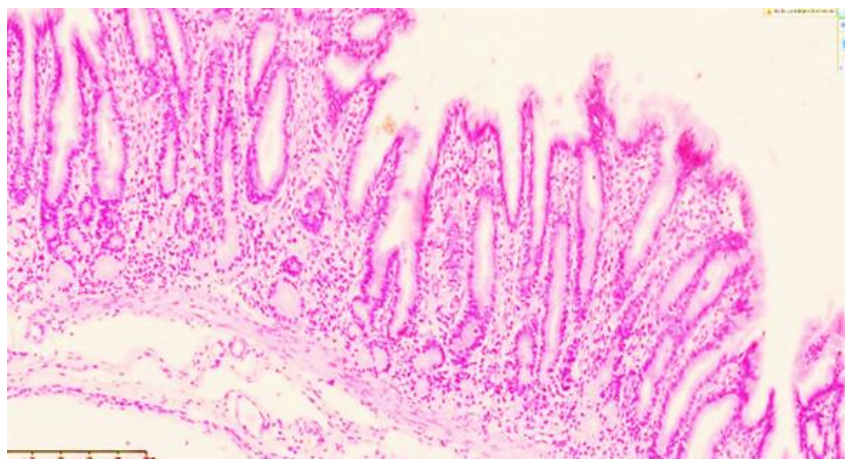




Figure 1. Gastric tissue from a 33-year-old male patient weighing 143 kg who underwent bariatric surgery. The gastric mucosa shows uneven thickness with areas of thinning. Numerous foci of lymphocytic infiltration are seen in the stroma. H&E staining. Magnification $\times 100$.

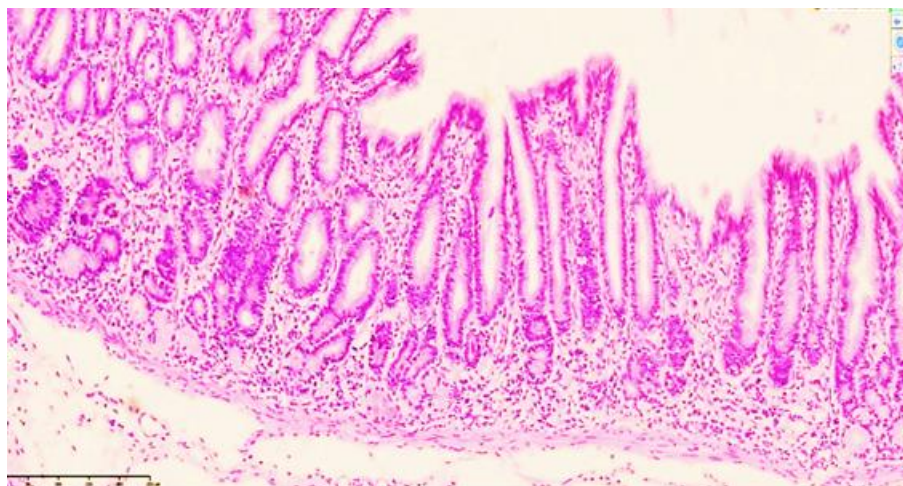


Figure 2. Gastric tissue from a 38-year-old male patient weighing 128 kg who underwent bariatric surgery. Atrophic and sclerotic changes are seen in the glands of the gastric mucosa. A large amount of secretion is present in the glandular lumens. The mucosa has uneven thickness

In men aged 45–59 years, the morphological changes were more pronounced. The gastric mucosa became thinner, and the number and size of the fundic glands decreased. Atrophic and dystrophic changes were more common in the glandular epithelium, parietal cells, and chief cells. In some areas, the glandular lumen became narrow and the epithelial cells were flattened. These findings suggested a decrease in secretory activity.

The amount of connective tissue in the mucosal stroma also increased. Foci of sclerosis and fibrosis were seen in several areas. The walls of small blood vessels became thicker, and some capillaries showed homogeneous changes and perivascular fibrosis. These findings suggest that microcirculatory disorders in the gastric mucosa became more marked with age.

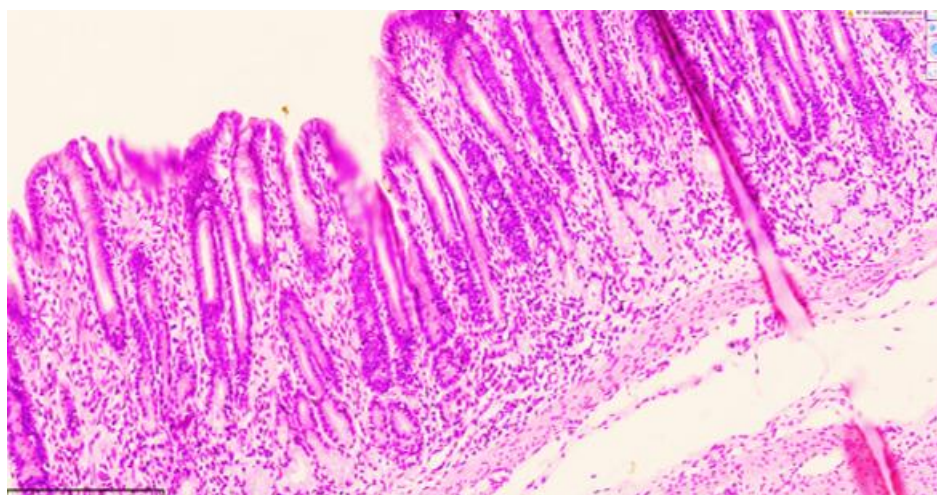


Figure 3. Gastric tissue from a 51-year-old male patient weighing 115 kg who underwent bariatric surgery. Atrophic and sclerotic changes are seen in the gastric glands and mucosal crypts. The mucosa is thinned in several areas, with structural



changes in the glands. Focal thickening of the basal layer is also seen at the border between the mucosa and submucosa. H&E staining. Magnification $\times 100$.

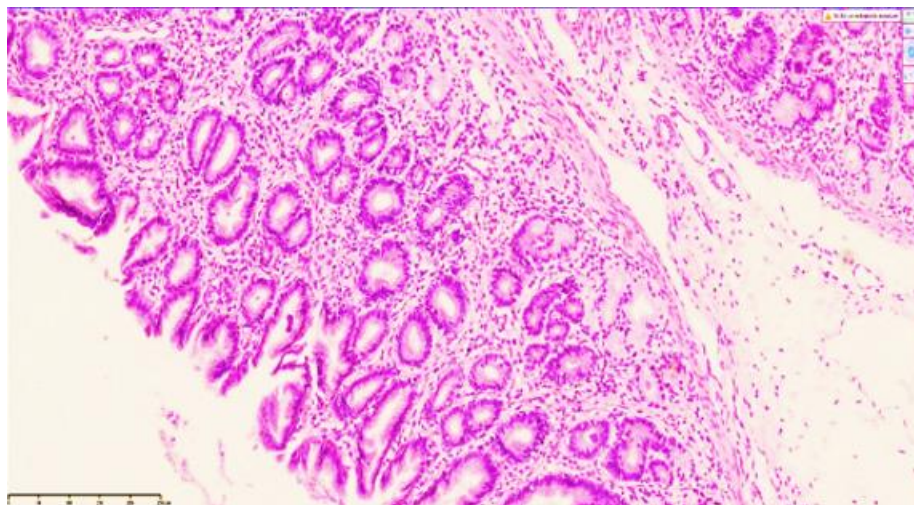


Figure 4. Gastric tissue from a 54-year-old male patient weighing 151 kg who underwent bariatric surgery. Atrophic and sclerotic changes are seen in the glands of the gastric mucosa. The mucosa is thinned in some areas, and focal thickening of the basal layer is present at the border between the mucosa and submucosa. H&E staining. Magnification $\times 100$.

In women aged 18–44 years, the general structure of the gastric mucosa was mostly preserved. Mild dystrophic changes were seen in the surface epithelium. In some areas, vacuolization and slight desquamation were present. The lamina propria showed focal lymphocytic infiltration, mild edema, and uneven blood filling of small vessels.

The fundic glands were also relatively well preserved in this age group. Marked atrophic changes were uncommon. Mild dystrophic changes were seen in parietal and chief cells. Some samples showed dilated capillaries and a small amount of inflammatory cell infiltration in the stroma. In general, the changes in younger women were mild and mostly limited to early inflammatory and microcirculatory disturbances.

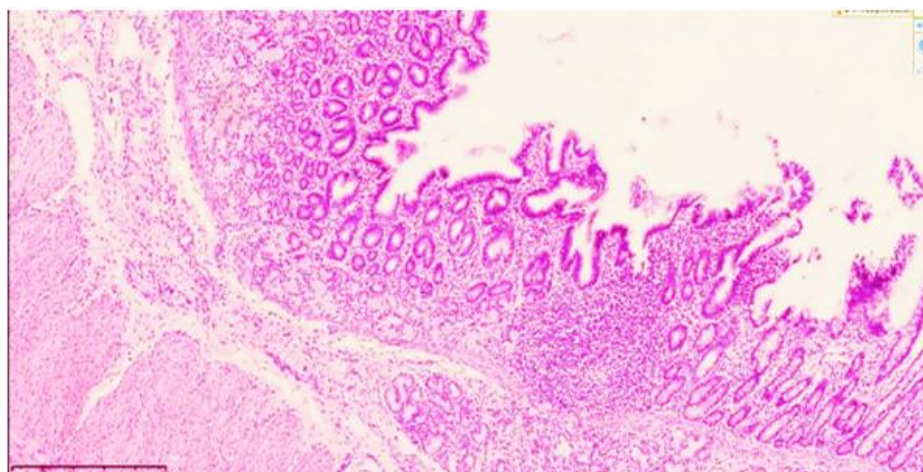


Figure 5. Gastric tissue from a 41-year-old female patient weighing 131 kg who underwent bariatric surgery. Focal atrophic and sclerotic changes are seen in the gastric glands. Local thickening of the basal layer is present at the border between the mucosa and submucosa. H&E staining. Magnification $\times 100$.

In women aged 45–59 years, the gastric mucosal changes were much more evident. The mucosa became thinner, and the fundic glands were less dense. Atrophic changes were seen in several glands. Dystrophic changes in the surface and glandular epithelium were also more common, with flattening of epithelial cells and signs of reduced secretory activity. The stroma contained more connective tissue, and areas of fibrosis and sclerosis were more frequent. The walls of small blood vessels were thicker, while some areas showed perivascular

fibrosis and signs of impaired microcirculation. Apoptotic changes in epithelial cells were also more common in this age group. A clear age-related difference was seen between the two female groups. The gastric mucosa remained relatively preserved in women aged 18–44 years, whereas women aged 45–59 years showed more severe atrophy, fibrosis, vascular changes, and epithelial damage. This pattern suggests that the gastric mucosa becomes more vulnerable to metabolic disturbances with increasing age.

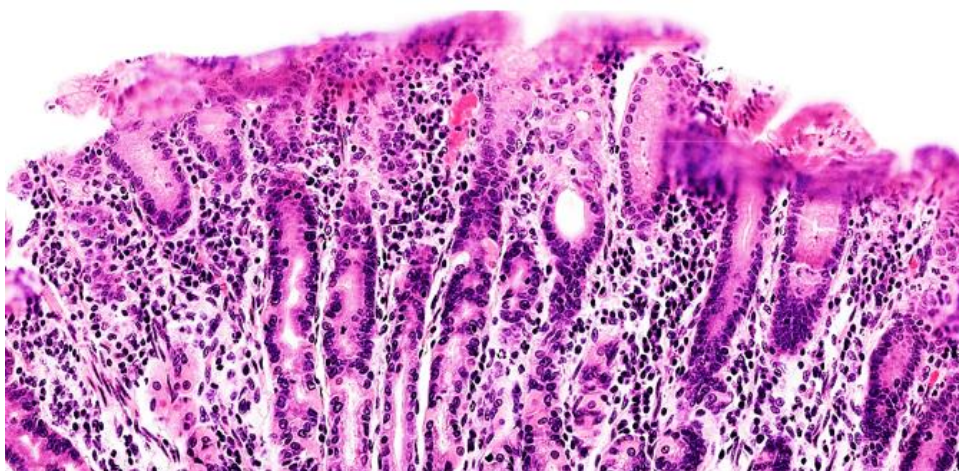


Figure 6. Gastric biopsy from the antral region of a 56-year-old female patient (biopsy No. 19/11). In the cross-section of the mucosa and folds, the glandular epithelial cells are reduced in size. Marked lymphocytic infiltration is seen in the stroma. Proliferative foci of lymphocytes and histiocytes are also present in the stroma. H&E stain. Magnification $\times 100$.

In men aged 18–44 years, the total thickness of the gastric mucosa was $845.2 \pm 24.1 \mu\text{m}$. In men aged 45–59 years, it decreased to $612.4 \pm 18.3 \mu\text{m}$. The volume density of the fundic glands also decreased from $42.6 \pm 1.8\%$ to $32.1 \pm 1.4\%$. The height of the surface epithelium fell from $28.4 \pm 0.9 \mu\text{m}$ to $19.2 \pm 0.7 \mu\text{m}$.

Age-related changes were also seen in the stroma and small blood vessels. The interglandular stromal area increased from $24.1 \pm 1.2\%$ in younger men to $34.8 \pm 1.5\%$ in the older group. Capillary wall thickness increased from $2.8 \pm 0.15 \mu\text{m}$ to 3.9 ± 0.22

μm . These changes showed that fibrosis and vascular wall thickening became more pronounced with age.

Lymphocytic infiltration decreased from 412.3 ± 15.4 cells/ mm^2 in men aged 18–44 years to 315.6 ± 12.1 cells/ mm^2 in men aged 45–59 years. At the same time, the epithelial apoptosis index increased from $4.2 \pm 0.3\%$ to $9.6 \pm 0.6\%$. This means that in older men, atrophic and degenerative changes became more prominent than inflammatory changes.

Table 1.

Morphometric parameters of the gastric mucosa in men with metabolic syndrome according to age group.

No.	Morphometric parameters	Men aged 18–44 years ($M \pm m$)	Men aged 45–59 years ($M \pm m$)	Unit
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1	Total thickness of the gastric mucosa	845.2 ± 24.1	612.4 ± 18.3	µm
2	Volume density of fundic glands	42.6 ± 1.8	32.1 ± 1.4	%
3	Height of the surface epithelium	28.4 ± 0.9	19.2 ± 0.7	µm
4	Thickness of the lamina propria	210.5 ± 8.4	165.3 ± 6.2	µm
5	Interglandular stromal area	24.1 ± 1.2	34.8 ± 1.5	%
6	Thickness of the submucosa (tela submucosa)	195.4 ± 7.6	142.1 ± 5.8	µm
7	Capillary wall thickness	2.8 ± 0.15	3.9 ± 0.22	µm
8	Lymphocytic infiltration of the gastric mucosa	412.3 ± 15.4	315.6 ± 12.1	cells/mm ²
9	Area of mucus-producing cells	18.5 ± 0.8	12.3 ± 0.5	% of total area
10	Epithelial cell apoptosis index	4.2 ± 0.3	9.6 ± 0.6	%

In women aged 18–44 years, the gastric mucosa was relatively well preserved. The total mucosal thickness was 890.5±21.3 µm, while the volume density of the fundic glands was 44.2±1.5%. The height of the surface epithelium was 30.1±0.8 µm, and the thickness of the lamina propria was 225.3±7.9 µm. These values were higher than those found in women aged 45–59 years. In the older female group, clear atrophic changes were seen. The total mucosal thickness decreased to 585.4±16.1 µm, and fundic gland density fell to 29.8±1.2%. The height of the surface epithelium also decreased to 17.4±0.6 µm. The lamina propria became thinner and measured 152.1±5.4 µm. The stromal component changed in the opposite direction. The interglandular stromal area increased from 21.6±1.1% in women aged 18–44 years to 38.4±1.6% in women aged 45–59 years. At the same time, the thickness of the submucosa decreased from 204.1±6.8 µm to 131.5±5.2 µm. Changes in small blood vessels were also more pronounced in the older group. Capillary wall thickness increased from 2.4±0.11

µm to 4.2±0.25 µm. This finding was consistent with the vascular and fibrotic changes seen on histological examination. Lymphocytic infiltration was higher in younger women and reached 435.8±14.2 cells/mm². In women aged 45–59 years, it decreased to 290.3±11.4 cells/mm². The area of mucus-producing cells also decreased, from 19.8±0.7% to 10.5±0.4%. The epithelial apoptosis index showed the opposite pattern. It increased from 3.8±0.2% in women aged 18–44 years to 11.4±0.8% in women aged 45–59 years. This was one of the clearest age-related changes in the female group.

Overall, younger women had thicker mucosa, better-preserved fundic glands, a higher surface epithelium, and more mucus-producing cells. In women aged 45–59 years, mucosal thinning, stromal expansion, capillary wall thickening, loss of glandular structures, and increased epithelial apoptosis were much more evident.

Table 2.

Morphometric parameters of the gastric mucosa in women with metabolic syndrome according to age group

No.	Morphometric parameters	Women aged 18–44 years (M ± m)	Women aged 45–59 years (M ± m)	Unit
1	Total thickness of the gastric mucosa	890.5 ± 21.3	585.4 ± 16.1	µm
2	Volume density of fundic glands	44.2 ± 1.5	29.8 ± 1.2	%
3	Height of the surface epithelium	30.1 ± 0.8	17.4 ± 0.6	µm
4	Thickness of the lamina propria	225.3 ± 7.9	152.1 ± 5.4	µm
5	Interglandular stromal area	21.6 ± 1.1	38.4 ± 1.6	%

6	Thickness of the submucosa	204.1 ± 6.8	131.5 ± 5.2	μm
7	Capillary wall thickness	2.4 ± 0.11	4.2 ± 0.25	μm
8	Lymphocytic infiltration of the gastric mucosa	435.8 ± 14.2	290.3 ± 11.4	cells/mm ²
9	Area of mucus-producing cells	19.8 ± 0.7	10.5 ± 0.4	% of total area
10	Epithelial cell apoptosis index	3.8 ± 0.2	11.4	

iNOS expression was evaluated in men with metabolic syndrome to assess oxidative stress in the gastric mucosa. In men aged 18–44 years, iNOS expression was generally low. A weak positive reaction was seen in some epithelial cells and around

small blood vessels. Strong staining was uncommon in this age group. These findings suggest that oxidative stress was present, but it was still limited.

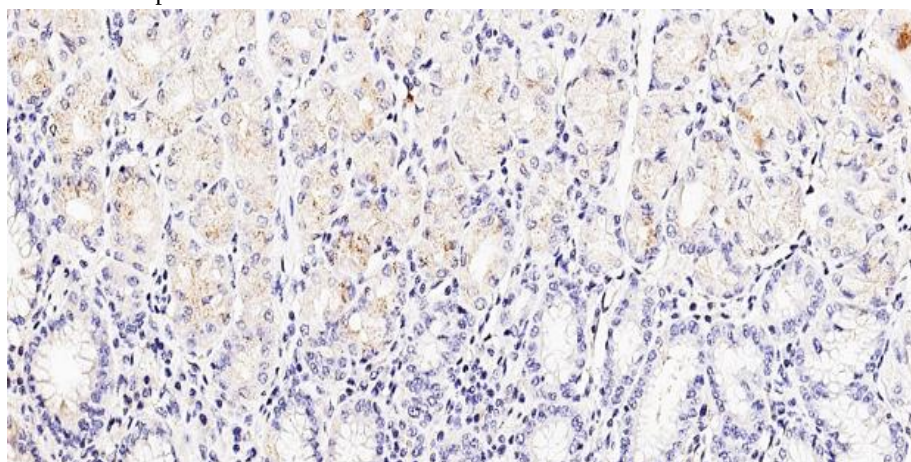


Figure 7. Gastric tissue from a 36-year-old man with metabolic syndrome. Low positive iNOS staining is seen. According to the Remmele and Stegner (2004) scale, the reaction was evaluated as negative. DAB chromogen staining. Magnification $\times 100$.

In men aged 45–59 years, iNOS expression was more noticeable. Moderate positive staining was seen in the gastric epithelium, glands, and around blood vessels. In some areas, the reaction was strong. Compared with younger men, this group showed a clear increase in iNOS activity.

The results showed that iNOS expression increased with age in men with metabolic syndrome. This increase was accompanied by more marked structural changes in the gastric mucosa, including atrophy, fibrosis, and vascular changes.

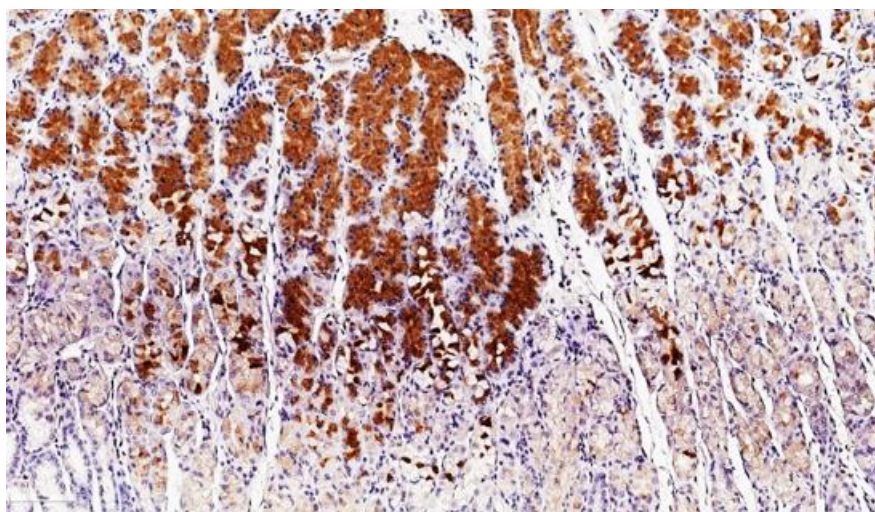


Figure 8. Gastric mucosa from a 49-year-old man in Group 2. Moderate to high positive iNOS expression is seen according to the Remmele and Stegner (2004) scale. Dark brown staining is present in the cytoplasm of surface and secretory cells of the fundic glands. DAB chromogen staining. Magnification $\times 100$.

In women aged 18–44 years, iNOS staining was mostly negative or weakly positive. Light brown staining was seen only in some epithelial and glandular cells. In most samples, the reaction remained low, and strong expression was rare. The

fundic glands were generally better preserved, and the vascular reaction was also mild. These findings suggest that oxidative stress was present in this age group, but it was not strongly expressed.

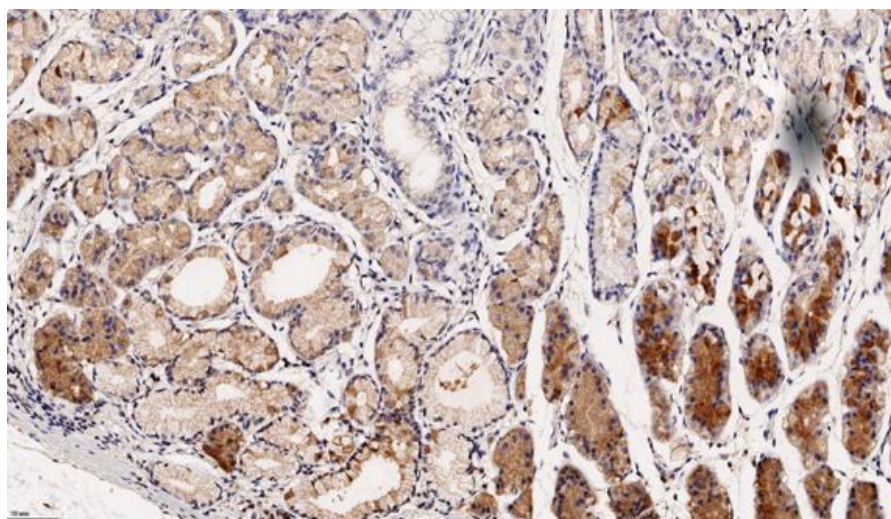


Figure 9. Gastric mucosa of a 35-year-old female patient with metabolic syndrome. Moderate positive expression of the iNOS marker was detected according to the Remmele and Stegner (2004) scale. Dark brown staining was seen in the cytoplasm of the covering and secretory cells of the fundic glands. DAB chromogen stain. Magnification 10×10 .

In women aged 45–59 years, iNOS expression became much more pronounced. Moderate and strong positive staining was seen in many epithelial cells, glandular structures, and in areas around small blood vessels. The cytoplasm of some

glandular cells showed dark brown staining, indicating a higher level of iNOS expression. These changes were more evident than those seen in younger women.

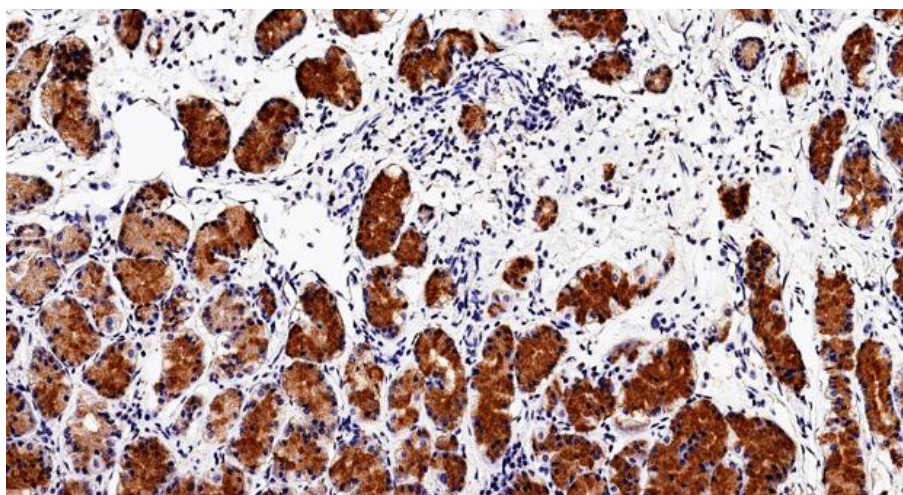


Figure 10. Gastric mucosa of a 58-year-old female patient with metabolic syndrome. High positive iNOS expression was detected according to the Remmele and Stegner (2004) scale. Dark brown staining was seen in the cytoplasm of fundic gland cells. DAB chromogen stain. Magnification 10×10.

The increase in iNOS expression in the older female group was accompanied by more marked morphological changes in the gastric mucosa. Atrophy of the glands, stromal fibrosis, vascular wall thickening, and epithelial damage were more common in this age group. This suggests that oxidative stress became more intense with age and may have contributed to the structural damage of the gastric mucosa.

CAIX expression also showed age-related differences in the gastric mucosa of patients with metabolic syndrome.

In men aged 18–44 years, CAIX staining was usually absent or weak. Only a small number of epithelial and glandular cells showed a light positive reaction. In most samples, the expression remained low. This means that signs of tissue hypoxia were still limited in younger men.

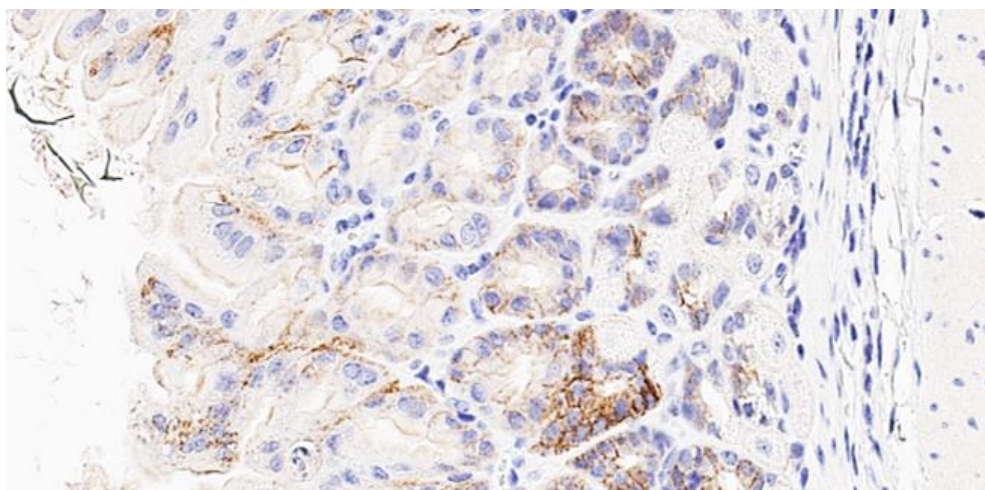


Figure 11. Gastric tissue from a 40-year-old male patient. A low positive reaction for the CAIX marker was observed. The expression was mainly seen focally in some glandular epithelial cells and stromal cells. DAB chromogen stain. Magnification 10×10.

In men aged 45–59 years, CAIX expression became more evident. Moderate positive staining was seen in the surface

epithelium and in the cells of the fundic glands. In some areas, the reaction was stronger. These findings suggest that local

hypoxia and changes in tissue metabolism became more pronounced with age.

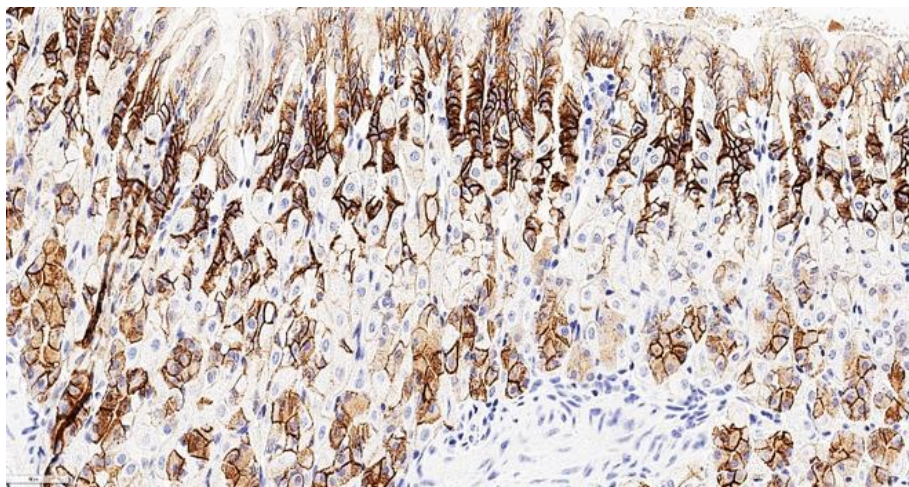


Figure 12. Gastric tissue from a 54-year-old male patient. High positive CAIX expression was seen in the cytoplasm of glandular epithelial cells in the antral region. The reaction was mainly observed in the glandular epithelium and was scored as 3 points according to the Remmele and Stegner (2004) scale. DAB chromogen stain. Magnification 10×10.

A similar pattern was found in women. In women aged 18–44 years, CAIX expression was mostly negative or weakly positive. The gastric mucosa was relatively well preserved, and strong staining was uncommon. In women aged 45–59 years, CAIX expression increased clearly. Strong positive staining was

seen in many epithelial and glandular cells. The reaction was more intense in areas where atrophy, fibrosis, and vascular changes were also present. This group showed the highest CAIX expression among the studied patients.

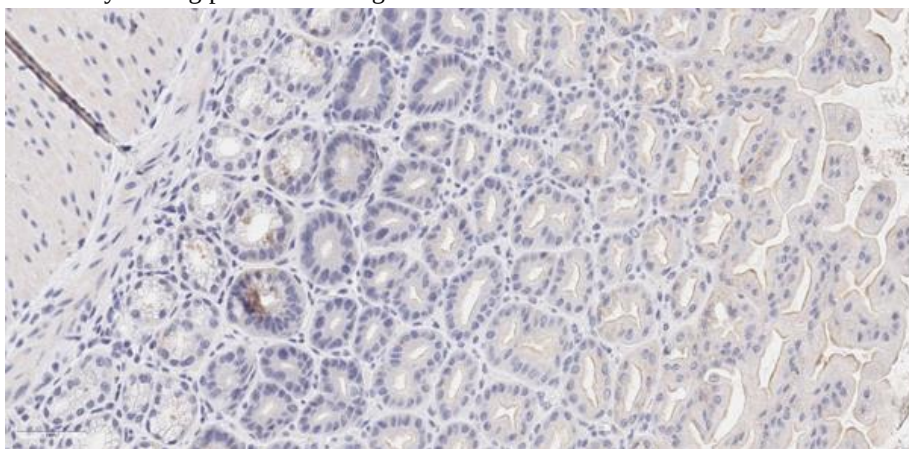


Figure 13. Gastric tissue from a 39-year-old female patient. No CAIX expression was detected. The reaction was scored as 0 according to the Remmele and Stegner (2004) scale. DAB chromogen stain. Magnification 10×10.

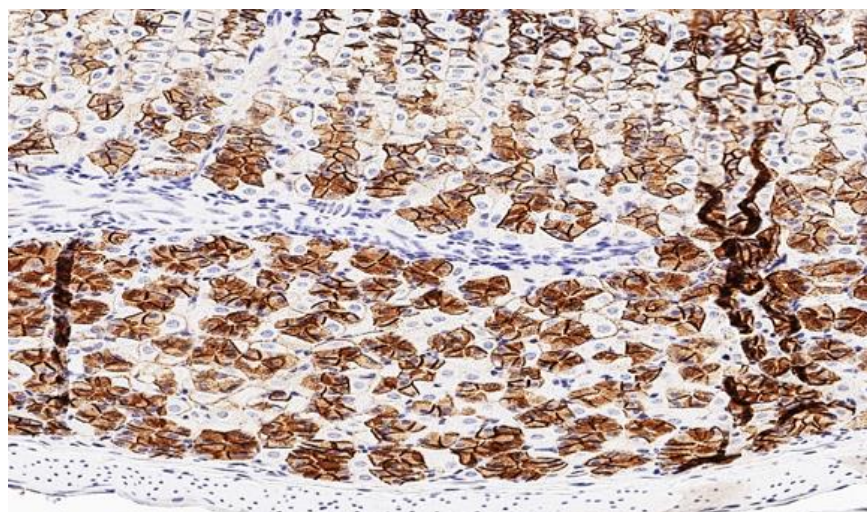


Figure 14. Gastric tissue from a 54-year-old female patient. High positive CAIX expression was seen on the membranes of glandular epithelial cells in the antral region, with a honeycomb-like staining pattern. The reaction was scored as 2 points according to the Remmele and Stegner (2004) scale. DAB chromogen stain. Magnification 10×10.

The increase in CAIX expression with age suggests that hypoxic changes in the gastric mucosa became stronger in metabolic syndrome. These changes were especially marked in women aged 45–59 years.

Overall comparison showed clear age-related changes in the gastric mucosa of both men and women with metabolic syndrome. In the 18–44-year group, the mucosa was generally better preserved, and the changes were mostly mild. In patients aged 45–59 years, mucosal thinning, loss of fundic glands, fibrosis, and vascular changes became more noticeable. These changes were stronger in women than in men of the same age. iNOS and CAIX expression also increased with age. The highest expression of both markers was seen in women aged 45–59 years. This suggests that oxidative stress and tissue hypoxia became more pronounced with age, together with structural damage of the gastric mucosa.

4. Discussion

The present study showed that metabolic syndrome is associated with clear structural changes in the gastric mucosa. These changes were not the same in all patients. Age and sex had an important influence on the severity of mucosal damage.

In younger patients, especially those aged 18–44 years, the gastric mucosa was relatively well preserved. The main findings were mild inflammation, epithelial dystrophy, edema, and early microcirculatory changes. In older patients, these changes became more severe. Mucosal thinning, glandular

atrophy, stromal fibrosis, vascular wall thickening, and increased epithelial apoptosis were more common.

The morphometric findings supported the histological observations. In both men and women, mucosal thickness and fundic gland density decreased with age. At the same time, the stromal area and capillary wall thickness increased. These changes suggest that chronic metabolic stress gradually affects both the epithelial and vascular parts of the gastric mucosa.

The age-related differences were especially clear in women. Women aged 18–44 years had relatively better-preserved mucosal structure. In contrast, women aged 45–59 years showed more marked atrophy, fibrosis, vascular changes, and apoptosis. This may be related to age-associated hormonal and metabolic changes, although this relationship requires further study.

The immunohistochemical findings were also consistent with the morphological results. iNOS expression increased in older patients, indicating stronger oxidative stress. CAIX expression also became more pronounced with age, suggesting greater tissue hypoxia. The highest expression of both markers was seen in women aged 45–59 years. Taken together, these findings show that metabolic syndrome can gradually damage the gastric mucosa. The process appears to become more pronounced with age and is especially evident in women after the age of 45.

5. Conclusion

Metabolic syndrome was associated with clear age-related changes in the gastric mucosa. In younger patients, the



changes were mainly mild and included inflammation, epithelial dystrophy, edema, and early vascular disturbances.

In patients aged 45–59 years, glandular atrophy, stromal fibrosis, vascular wall thickening, mucosal thinning, and epithelial apoptosis became more pronounced. These changes were especially evident in women.

The increase in iNOS and CAIX expression with age showed that oxidative stress and tissue hypoxia were closely related to the structural damage of the gastric mucosa. The highest expression of both markers was found in women aged 45–59 years.

These findings show that age and sex should be considered when evaluating gastric mucosal changes in patients with metabolic syndrome.

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