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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

COMPARATIVE EVALUATION OF THE RESULTS OF ENDOSCOPIC AND HISTOMORPHOLOGICAL STUDIES IN PATIENTS WITH GASTROINTESTINAL COMPLAINTS

Speciality: 3205.01 – Internal diseases

Field of science: Medicine

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The work was performed at the Department of Therapeutic and Pediatric Propaedeutic of Azerbaijan Medical University

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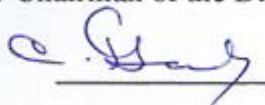Official opponents: Doctor of medical sciences, professor
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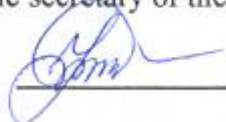   **Geyrat Museyib Imamaliyev**

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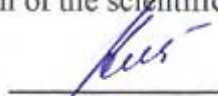   Doctor of medical sciences, professor
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GENERAL DESCRIPTION OF THE WORK

The relevance of the topic. The study of the occurrence and spread of oncological and other diseases among the population, the identification of high-risk groups, the development of action plans on age, sex and geographical area is additionally vital for our country.

Both clinical and epidemiological, as well as other scientific research and studies, as well as relevant information from various sources, are very important for this work which carried out in this area during the development, implementation of national programs aimed at disease control, and objective evaluation of the work done[1].

Because in recent years there has been a huge expansion in oncological diseases of the gastrointestinal tract, so the incidence of esophageal cancer and cancer of the cardiac part of the stomach in the United States has increased by 400%.

The disease is 8 times more common in men than in women, and 5 times more common in whites race than in black race[2,3].

In this country, colorectal cancer (CRC) is detected in the case 68% after metastasis to surrounding lymph nodes and in 10% to other organs[4]. In our country, when cancer of the descending colon and recto-sigmoidal area is detected, in the case of 68% are already infected with the surrounding tissues[5].

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[1]*Əliyev, C.Ə.* Xərçəngin qeydiyyatında populyasiya xərçəng registrinin rolu / C.Ə.Əliyev, Ə.C.Əliyev, F. A.Mərdanlı [and başq.] // – Bakı: Azərbaycan Onkologiya and Hematologiya Jurnalı, – 2015. №1, – s. 103-105.

[2]*Dubecz , A.* Does the incidence of adenocarcinoma of the esophagus and gastric cardia continue to rise in the twenty-first century? a SEER database analysis / A.Dubecz, N.Solymosi, R.J.Stadlhuber [et al.] // J. Gastrointestinal Surgery, –2013. Nov; 15. 18(1). doi:10.1007/s11605-013-2345-8

[3]*Evans, J. A.* The role of endoscopy in the assessment and treatment of esophageal cancer (Guideline of ASGE) / J. A.Evans, D.S.Early, V.Chandrasekhara [et al.] // Gastrointestinal Endoscopy, – 2013. 77(3), – p. 328-334.

[4]*Levin, B.* Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps / B.Levin, D. A.Liberman, B.McFarland [et al.] // CA Cancer J. Clin., – 2008. 58, – p. 130-160.

[5]*Kərimov, Ə.X.* Enən and rektosiqmoid bağırsaq xərçənginin ətraf orqanlara invazi-yası zamanı cərrahiyyə müalicəsinin taktikasının seçimi / Ə.X.Kərimov, N.Ə.Əskə-rov, Y.R.Əliyarov [and başq.] // – Bakı: Azərbaycan Onkologiya Jurnalı, – 2017. №2, – s. 72-74.

Therefore, as in the remainder of the world, the most important modern strategic direction in the fight against cancer in Azerbaijan is the early diagnosis and adequate treatment of both oncological diseases and precancerous conditions[6].

Thus, endoscopic examination based on gastrointestinal complaints (GIC) and symptoms, and histopathological examination of the biopsy material taken in this case, play a crucial role in making a correct diagnosis in many cases and determine the optimal framework for both therapeutic and prophylactic measures and therefore scientific research in this area is very relevant.

The degree of use of the topic. Analysis of the literature showed that in our country, there are very few studies that reflect the analysis of the results of endoscopic and histomorphological examinations of those who apply to the hospital with a therapeutic profile with gastrointestinal complaints.

Specifically, the reliability, proportionality, strength and odds ratio of pathologies of the statistical correlation between individual gastrointestinal complaints and the results of endoscopic examinations are the least studied scientific direction not only in our country but in the entire world.

Object and subject of the research. Object of the research were patients with gastrointestinal complaints. Clinically, research is devoted to the investigation of the characteristics correlation between gastrointestinal complaints and endoscopic and histomorphological diagnoses.

The purpose of the research: means comparative study of the types of pathologies revealed by endoscopic and histomorphological examinations of individuals with gastrointestinal complaints, the frequency of occurrence, the prevalence rate, age and sex characteristics, as well as to evaluate the statistical correlation between the complaint and the endoscopic result from the point of view of diagnostic criteria for or against individual diseases of the tubular organs of the digestive system.

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[6]*Алиев, Д.А., Мамедов, М.К. Основные направления современной стратегии противораковой борьбы // – Bakı: Azərbaycan Onkologiya Jurnalı, – 2013. №1, с. 1-8.*

Research objectives:

1. To study of the types of malignant tumors and other pathologies detected in patients with gastrointestinal complaints and those undergoing endoscopic examination for control without complaints, the frequency of occurrence in the population, sex and age characteristics;

2. Biopsies and to evaluate the histomorphological features of the pathological lesion of the mucous membrane of the esophagus, stomach, duodenum, colon and rectum, based on the results obtained, to demonstrate the importance of histomorphological examination in both pre-cancerous conditions and early detection of cancer;

3. To study of the possibility of individual complaints in favor of or against the diagnosis of various diseases of the tubular organs of the digestive system, based on the strength, reliability, odds ratio, probability and proportionality of the statistical correlation between gastrointestinal complaints and the results of endoscopic examination;

4. To study of the correlation of extraoral halitosis with pathologies of the tubular organs of the digestive system, which has recently become a major cause of gastrointestinal complaints;

5. To study of the propagation frequency of polyps and cancer of colon and rectum among the population belonging to different age groups on decades. Based on the results obtained, to substantiate which decade the most suitable age group for the detection of polyps and cancer by colonoscopy in the population of Azerbaijan.

Research methods. During the research, diagnostic esophago-gastro-duodenoscopy (EGD) and colonoscopy, urease and Campylobacter-like organism (CLO) tests for the detection of *Helicobacter pylori* infection, biopsies from the pathological lesion of the mucous membrane of the tubular organs of the gastrointestinal tract and histomorphological methods of examination were used.

Main thesis of dissertation for defense:

− In our country, incidence of cancer in the esophagus, stomach, colon and rectum of patients with gastrointestinal complaints who are admitted to the clinic with a therapeutic profile and underwent endoscopic examination on medical grounds is many times higher than similar indicators for the general population.

Frequency of occurrence of cancer which found in the tubular organs of the digestive system by endoscopy increases significantly in the next decades of age.

− Histomorphological examination of biopsies taken from pathological lesions of the mucous membrane in the form of malignant tumors on endoscopic examination allows to reveal that a significant part of these tumors is in the pre-cancer stage (pathological regeneration, increased mitotic activity and varying degrees of dysplasia), and some in the earliest stage of cancer ("carcinoma *in situ*").

− Indicators such as the reliability, proportionality, odds ratio and strength of the statistical correlation between individual gastrointestinal complaints and various diseases recognized by endoscopic examination can be considered as diagnostic criteria for or against many diseases of the tubular organs of the digestive system.

− Duodenogastric reflux is one of the causes of extraoral halitosis (bad breath, which is not related to the pathology and hygiene of the oral cavity, felt at certain intervals).

− The most suitable age for the search of polyps by colonoscopy method (screening) in the Azerbaijani population is in the IV decade, and the most suitable age for search of cancer is in the V decade.

Scientific novelty of the research:

− For the first time in our country, individual pathologies detected by endoscopy of patients who applied to therapeutic profile hospitalization with gastrointestinal complaints and those examined for control without any complaints were grouped according to the frequency of occurrence (less than 1%, between 1-10% and more than 10%), and characteristics were determined according to age and sex.

− For the first time, it was shown that the statistical correlation between gastrointestinal complaints and endoscopic outcome can be assessed as a criterion for or against various diseases, from a diagnostic point of view.

− For the first time, the fact that duodenogastric reflux is one of

the causes of extraoral halitosis has been scientifically, statistically and practically proven.
- The results obtained by histopathological examination of biopsy materials taken from the mucous membrane were analyzed comparatively with the endoscopic diagnosis, the role of both methods in the early diagnosis of cancer of the gastrointestinal tract has been shown.
- For the first time, it has been practically substantiated that the most suitable age group for the search for polyps and cancers of the colon (large intestine) and rectum in the population of the country is in the IV and V decades, respectively.

Practical significance of the research. The study examined the detected pathologies found in the esophagus, stomach, duodenum, colon and rectum by endoscopic examination method in a group of people applying to hospitals with a therapeutic profile with gastrointestinal complaints in our country: It allowed grouping and classifying more than 10%, those occurring between 1% and 10%, and those less than 1%. In addition, the age and sex characteristics of these pathologies are visually shown.

During the implemented scientific research, using indicators such as the reliability of the statistical correlation between gastrointestinal complaints and the results of endoscopic examinations, odds ratio, proportionality and strength and it has shown that it can be evaluated as a diagnostic criterion from a positive or negative point of view for various diseases of the tubular organs of the digestive system of individual complaints. This approach is a new direction for scientific research and it is also has great theoretical and practical importance.

Research has shown that duodenogastric reflux is one of the causes of extraoral halitosis, and it is necessary to continue scientific research in this field.

As a result of histomorphological examinations revealed that, although colonoscopic examination of the colon during chronic diarrhea shows a normal appearance, the cause of chronic diarrhea in a significant proportion of these patients is lymphocytic colitis.

The frequency of occurrence of colon polyps is almost the same in the Azerbaijani population, both in patients with gastrointestinal

complaints and in those who have no complaints and feel virtually healthy.This fact is evidence that unaggravated polyps of the colon (large intestine) are asymptomatic.

Endoscopic and histopathological examinations are very important for the early diagnosis of existing cancer and precancerous conditions in individuals who has gastrointestinal complaints.

Approbation. The main provisions of the research were presented at the following scientific conferences: IV International Medical Congress (Baku, Nov. 2-3, 2017); 34. National Gastroenterology Week (Antalya, Dec. 1-6, 2017); "XXII Republican Scientific Conference of Doctoral Students and Young Researchers" of the Ministry of Education of the Republic of Azerbaijan (Baku, Nov. 22-23, 2018).

The main provisions of the dissertation were reported and discussed at the interdepartmental meeting meeting of the Azerbaijan Medical University (March 15, 2019, protocol № 02) and at the scientific seminar of the Dissertation Council ED 2.27 operating at Azerbaijan Medical University (May 25, 2021, protocol № 03).

Application of research results: The results of the study were applied in the Educational Therapeutic Clinic of the Azerbaijan Medical University.

The name of the organization where the dissertation has been accomplished. The research was performed at the Department of therapeutic and pediatric propaedeutic of Azerbaijan Medical University.

Publications. Based on the materials of the dissertation, 15 scientific works reflecting the main content of the work, including 8 articles and 7 theses were published, of which 2 articles and 2 thesis were published abroad.

Volume and the structure of the dissertation. The dissertation consists of 269645 symbols. Title page - 398 characters; Table of contents - 4 pages 8745 characters; Introduction - 9 pages and 16270 characters; Chapter I - 31 pages and 61885 characters; Chapter II - 16 pages and 21698 characters; Chapter III - 25 pages and 36523 characters; Chapter IV - 23 pages and 32384 characters; Chapter V - 14 pages and 19414 characters; Chapter VI - 24 pages and 34985 characters; Discussion - 17 pages and 32225 characters; Results - 2

pages and 2560 characters; Practical recommendations - 1 page and 865 characters; List of abbreviations - 2 pages and 1603 characters The total volume of the dissertation is 202 pages.

The dissertation is visualized with 3 formulas, 27 tables, 38 charts. The list of references covers 238 sources. 12 of them are in Azerbaijani, 51-Turkish, 71 – Russian, and 104 - in englishe.

CHARACTERISTICS OF CLINICAL MATERIAL
AND RESEARCH METHODS

The dissertation covers the results of 1.409 persons ranging in age from 6 to 89 years, who underwent endoscopic examination by the researcher in 2015-2018 at the Oxygen, HAYAT Clinic and AMU Educational Therapeutic Clinic in Baku. EGD was performed in 1120 of them, and colonoscopy was performed in 289 of them. 1068 (552 men and 516 women) patients with upper gastrointestinal complaints (GIC) were included in the patients group (PG), and 52 people (17 men and 35 women) who were examined for control purposes without complaint were included in the control group (CG) (total 1120 patients). 241 people (73 men and 168 women) who applied with low GIC were referred to the PG for colonoscopy, 48 people (16 men and 32 women) who wanted to be examined for control purposes were included in the CG (a total of 289 patients).

During EGD, 2-8 biopsies were taken from mucous membrane with a pathological appearance of the upper digestive tract of 116 patients and taking from mucous membrane of the colon and rectum of 61 patients those underwent colonoscopy and was sent for histopathological examination.

Patients who underwent EGD examination, often applied to us with epigastric pain. The next places were occupied by belching (23.04%), regurgitation (19.46%), taste in the mouth (17.59%), swelling (14.02%), burning in the epigastrium (13.13%), early saturation (10.36%), discomfort in the epigastrium (9.91%), bad smell out of breath (6.93%), nausea (3.21%), vomiting (2.41%), difficulty swallowing (2.41%), painful swallowing (2.32%), melena (1.43%), feeling of heaviness in the stomach (1.25%), diarrhea of unknown

cause (0.63%), anemia of unknown cause (0.54%) and unexplained weight loss (0.54%).

The age range of 1068 patients in the PG ranged from 9 to 89 (average age 39.7±14.3 years). The age of 63 (5.9%) persons of them was between 9 and 20 years; The age of 276 (25.84%) persons was between 21 and 30 years; The age of 242 persons (22.66%) was between 31 and 40 years; The age of 235 people (22.0%) was between of 41 and 50 ages; The age of 166 people (15.54%) was between 51 and 60 years; The age of 86 people (8.05%) was between 61 and 89 years.

General characteristics of those who underwent colonoscopy

The age of the 289 people (89 men and 200 women) ranged from 6 to 83 years (average age 43.6±14 years) who underwent colonoscopy with complaints (PG) grouped under headings such as lower abdominal pain, hematochezia, chronic constipation, chronic diarrhea, and violation of the habit of defecation, as well as who underwent colonoscopy for the purpose of control (CG) without complaint.

PG consisted of 241 people (73 men and 168 women, average age 42.4±14.3 years), CG consisted of 48 people (16 men and 32 women, average age 49.6±10.6 years).

The vast majority of those who underwent colonoscopy suffered from chronic constipation, hematoxia, and and pain in the lower abdomen (87.6%).

Histomorphological examination of the biopsy was carried out under a "MOTIC" light microscope at a magnification of 56, 200 and 400 times. A biopsy sample taken from the gastric mucosa for HP was evaluated using the CLO test (tube with urease reagent or on plate - Pronto Dry® "GASTEREX", France) or cytologically during histopathological examination.

From the statistical parameters, the average calculated value (M), standard error of this indicator (m), average quadratic inclination (σ), minimum (min), maximum (max) values and 95% reliability intervals were calculated. The accuracy (p) of the difference between the achieved indicators of the groups was assessed by the non-parametric

Kruskal-Wallis criterion. We used the dispersion method (ANOVA) for comparison the indicators of more than two groups that are not interdependent. Share amount of indicators by percentage (P) and the mean error of percentage were also calculated. Pearson's eligibility criteria (χ^2) was used to statistically evaluate the figures obtained.

The strength (φ-quantity) of the statistical correlation between the indicators was calculated according to the four-digit tables. The correlation was evaluated as insignificant when the achieved result was between 0 and 0.1; when between 0.11 and 0.2 - as weak, between 0.21 and 0.4 - average; between 0.41 and 0.6 - relatively strong; higher than 0.61- as strong.

Statistical calculations of the dissertation work were performed in Excel 2010 spreadsheet and SPSS-20 package program.

RESEARCH RESULTS AND THEIR DISCUSSION

Frequency of occurrence of pathologies which detected in the esophagus

Esophagitis (34.6% and 13.4%), gastro-esophageal reflux disease (GERD - 27.5% and 15.5%) and esophageal hernia of the diaphragm (hiatal hernia) (EHD - 16.2% and 11.5%) (Chart 1) belongs to the patology which seen in esophagoscopy more than 10% in esophagoscopy of patients of control and patient group.
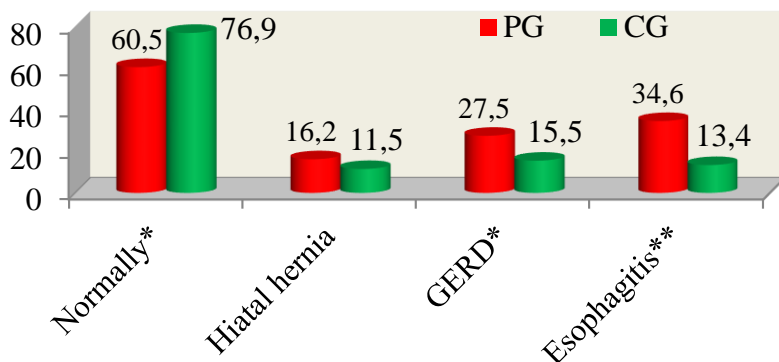
Note:* p<0.05; ** p<0.01

Chart 1. More than 10% pathologies seen in the esophagus and norm

The esophagus of 60.5% of patients in patients groups (PG) and of 76.9% of those in the control group (CG) was normal on endoscopy (p<0.01).

Results of histopathological examination of biopsies taken from pathological lesions of the esophagus

Generally, we met esophageal tumors in only 31 (2.8%) of 1120 patients during esophagoscopy. According to histopathological examination, the first place among these tumors is occupied by polyps (48%), the second place by cancer (29%), and the third place by leiomyoma (23%).

During the research, squamous cell carcinoma in 8.69%, undifferentiated carcinoma in 4.35%, and keratosis in 4.35% , morphologically, squamous epithelial dysplasia in 8.69% of the bioptates taken from the esophagus has been identified.

From the histopathological point of view, the first two of these pathologies are esophageal cancer, and the other two are precancerous. We found squamous papilloma, a benign esophageal tumor, in 17.39% of bioptates.

Hyperplasia of the esophageal mucosa in 13.04% of bioptates and accordingly squamous epithelial hyperplasia and hypertrophy of the mucous membrane in 4.35% was identified.

According to the results of histopathological examination, inflammation of the mucous membrane of unknown cause, erosive-ulcerative inflammation and inflammation of Candida origin respectively was available in 8.69% of biopsies.

Inflammation of cytomegalovirus origin and Barrett's esophagus was identified in 4.35% of bioptates. Thus, histopathologically, cancer and precancerous conditions were detected in 26.08% of tissue samples taken by biopsy method from the mucous membrane of the esophagus; polyp of flat epithelial origin, epithelial hyperplasia, hypertrophy and hyperplasia of the mucous membrane in 39.13% and inflammation of the mucous membranes of various origins in 34.77% also was detected.

Frequency of pathologies which revealed in the esophagus by age and sex

The research found that 73.4% of those in the ≤ 20 age group have a esophagus in normal condition. Among those aged 41-50, this figure is 56.2%; 56.1% in the sixth decade; In the seventh decade and older, it is 58% (p<0.05).

Esophageal cancer was found in 0.4% of those in the 41-50 age group, in 1.2% of those in the 51-60 age group, in 6.3% of those in the 61 age group (p<0.05).

Age-related variations of varicose veins in the esophagus: we saw as 1.2% in the 41-50 age group, 2.9% in the 51-60 age group, 6.3% in the age group of 61≥ (p<0.05).

GERD, one of the most common pathologies of the esophagus, was determined at a level very close to each other in almost all study groups. The highest result on this indicator is in the 21-30 age group (31.5%), the lowest result was recorded in the ≥ 61 age group (17.9%).

We encountered EHD at the level of 7.8% in the 20-year-old group, 13.6% in the 21-30 age group, and 22.5% in the 31-40 age group. The difference between these three groups is statistically significant (p<0.05). Indicators in other age groups were at the level of 14.45% and 15.5%.

In male patients, esophagitis (50.3%) and EHD (20.4%), related indicators were twice as high for women difference is statistically honest (p<0.001).

During the endoscopic study, we found a total of 22 tumors (5 leiomyomas - 0.9%; 10 polyps - 1.8%; 7 cancers - 1.2%) in the esophagus of 569 patients in the male group but In the group of 551 women, we saw only 9 tumors (2 leiomyomas - 0.4%; 5 polyps - 0.9%; 2 cancers - 0.4%).

As can be seen, esophageal cancer is 3 times (M/F=3/1) more common in male than in female, and leiomyoma and polyps are 2 times more common in our country (p<0.05).

The most common pathology in women than in men is varicose dilated veins in the esophagus and its frequency of occurrence in women is 12 times higher than in men (p<0.01).

Features of the correlation between upper GIC and esophageal pathology

In those with high GIC, there is an inverse proportionality between the normal position of the esophagus endoscopically (Table 1). Those with dyspeptic complaints have a 0.46 odds of a normal esophagus, which is statistically low ($p_1 < 0.05$) and this inverse proportionality is very strong ($\chi^2 = 5.64$; $p_2 = 0.018$).

There is a straight proportion and a statistically significant strong correlation among the upper GIC and diagnosis of esophagitis which detected on endoscopic examination. (CR=3.42; $p_1 < 0.05$; $\chi^2 = 10.04$; $p_2 = 0.002$). A similar situation was identified between the upper GIC and the GERD (CR=2.44; $p_1 < 0.05$; $\chi_2 = 4.99$; $p_2 = 0.025$). From the above, it becomes clear that people with high GIC are more prone to esophagitis and GERD on EGD.

Table 1

The correlation between esophageal pathologies odds ratio (OR), complaints and outcome

Diagnosis	OR	Correlation	p_1	χ^2	p_2
Norm	0.46	inverse	< 0.05[*]	5.64	0.018[**]
Esophagitis	3.42	straight	< 0.05[*]	10.04	0.002[**]
GERD	2.44	straight	< 0.05[*]	4.99	0.025[**]

Notes: 1. p_1 * - the difference is valid compared to the control group;
      2. p_2**- the correlation between complaint and pathology is statistically significant.

We have witnessed the existence of a statistically reliable, straight, and a correlation with a medium level of strength between halitosis in the background of the upper GIC and only GERD (OR=3.91; $\chi^2 = 9.04$; $p < 0.01$ and $\varphi = 0.268$).

Features of the correlation between "symptoms of anxiety" in the background of dyspepsia and pathology of the esophagus

53 of the 1068 patients who we examined an EGD for upper GIC, had "signs of anxiety" accompanied by dyspepsia, the remaining 1.015

patients were examined only for signs of dyspepsia (comparison group).

Patients with "signs of anxiety" against the background of dyspepsia are statistically significant less likely to have the odds to have normal esophagus than patients with dyspepsia alone, this correlation is inverse due to the feature, statistically accurate and although the strength is weak but is a negative prognostic criterion (OR=0.26; $p_1<0.05$; $\chi^2=21.42$; $p_2<0.001$; $\varphi=0.142$).

Due to its nature, the correlation between "signs of anxiety" and esophageal candidiasis is straight, statistically is accurate and because of its relative strength "signs of anxiety" against the background of dyspepsia are one of the main diagnostic criteria in favor of esophageal candidiasis (OR=265.7; $\chi^2=193.45$; $p_2=0.001$ and $\varphi=0.426$).

The odds ratio for esophageal ulcers of the neck, chest and abdomen in patients with "signs of anxiety" against the background of dyspepsia, respectively is equal to 52.7 and 10.5 ($p_1<0.05$).In ulcers of the neck and chest, the strength of this straight correlation is moderate ($\varphi=0.271$ and $\varphi=0.249$), but it is weak in abdominal ulcers ($\varphi=0.156$, in all three cases $p_2<0.001$). Therefore, "signs of anxiety" against the background of dyspepsia should be considered a prognostic criterion in favor of esophageal ulcers.

In patients with "signs of anxiety" against the background of dyspepsia, we found 52.76 times more cases of non-epithelial origin of the esophagus - leiomyoma, than those with dyspepsia alone (OR=52.76; $p_1<0.05$).

As can be seen, the correlation between leiomyoma and "signs of anxiety" in the background of dyspepsia is straight, statistically accurate, and the strength of this correlation is moderate ($\chi^2=66.0$; $p_2<0.001$; $\varphi=0.249$).

We have met 43.06 times more cases of cancer in people with "signs of anxiety" against the background of dyspepsia (OR=43.06; $p_1<0.05$). The analysis shows that, the correlation between esophageal cancer and "signs of anxiety" is straight, statistically accurate, and moderate ($\chi^2=73.27$; $p_2<0.001$; $\varphi=0.262$).

These indicators are sufficient to consider the "signs of anxiety" as

a prognostic criterion avor of in ffor both esophageal leiomyoma and cancer.

Frequency of ocurance of pathologies detected in the stomach

Mucous membrane of the stomach of 17.67% of patients of the PG, 49.02% of the persons of CG was assessed as normal in gastroscopy. (Chart 2) (p<0.001). The frequency of occurrence of gastritis is almost the same in both groups. The figure shows that, erosive gastritis (EG) - 2.8 times more than pathologies seen in more than 10% of patients in PG compared to CG, duodenogastric reflux (DGR) - 2.4 times, pyloric dysfunction (PD) is 6.15 times higher.

Gastric pathologies seen between 1% and 10% in PG and CG: were peptic ulcer (5.1% and 2%), polyp (2.7% and 9.8%), gastric cancer (1.8%) and reflux gastritis (7.4%). We did not find cancer or reflux gastritis in CG.

Less than 1% of the pathologies we encountered during gastroscopy were pyloric duct ulcers (0.5%), intramural mass in the stomach (0.5%), and 0.1% of each - angiodysplasia, varicose of the fundus veins and portal hypertension-related.
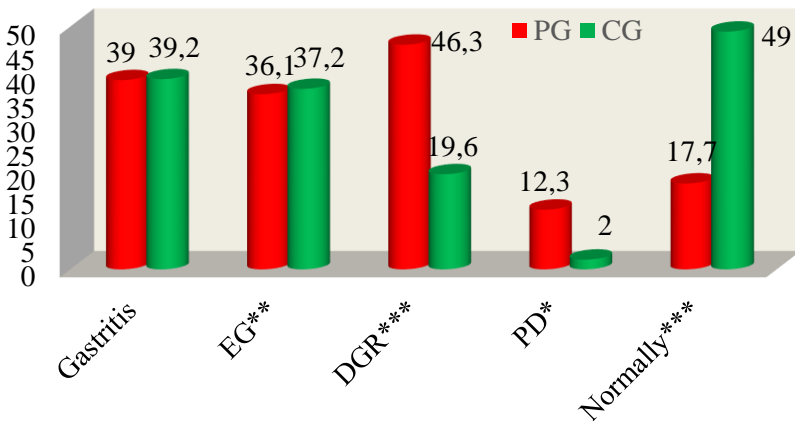
Note: * p<0.05; ** p<0.01; *** p<0.001.

Chart 2. Available pathologies more than 10% in the stomach and the norm

Results of histopathological examination of biopsies taken from the gastric mucosa for diagnostic purposes

During gastroscopy, bioptates taken from 116 individuals showed 2.6% type C gastritis, 4.3% had type B gastritis, 31% had inactivation of chronic gastritis, and 15.5% had chronic gastritis; Acute gastritis in 2.6%, polyps in 13.8%, xanthoma in 0.9%, intestinal metaplasia in the mucous membrane in 7.8%, glandular hyperplasia in 4.3%, hypertrophy of the diaphragm in 5.2% and atrophy in 12.1%. In addition, severe dysplasia in 44.4% of cases, "carcinoma *in situ*" in 11.1%, moderately differentiated carcinoma in 33.3%, and low-grade carcinoma in 11.1% was identified in the histopathological research of biopsies resembling a malignant tumor in endoscopic appearance and taken from 9 patients. Among the gastric polyps which we found out, tubular adenoma in the first place (50.0%), hyperplastic polyp in the second place (37.5%), later places there were fundus glandular polyps (6.25%) and villous adenomas (6.25%).
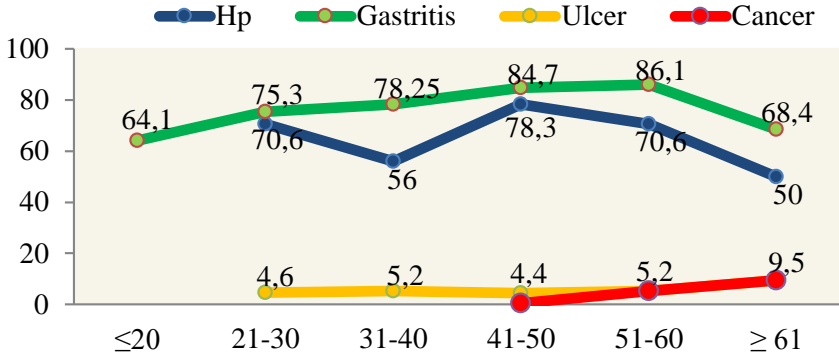
Frequency of occurrence of gastric pathologies according to age and sex

Non-atrophic gastritis was most common in the 31-40 age group (42.1%) and least common in the ≥61 age group (25.3%). We found reflux gastritis most in the ≤ 20 age group (9.4%) and at least in the 31-40 and 51-60 age groups (5.2%).

Erosive gastritis was most common in the 51-60 age group with a 45.35% incidence and 17.2%. were seen in the ≤20 age group at least. Gastric ulcer showing serious addiction from the age factor with 9.5%, the highest age was found in the ≥61 group.≤ In the age group of 20, we did not encounter this pathology. We saw ulcer of the pyloric canal only in the 21-30 (1.1%) and 41-50 (1.2%) age groups. DGR was also severely dependent on age,so it was seen in 60.9% of the ≤20 age group and only 35.5% in the ≥61 age group.

Gastric cancer was seen 0.4% in those aged 41-50, 5.2% in those aged 51-60, in the case of 9.5% In the ≥61 group (Chart 3). From the graph in this chart, it is clear that there is a parallel between the

indicators of encounter of Hp bacteria and the frequency of endoscopic detection of gastritis.

Chart 3. Frequency of occurrence Hp, gastritis, ulcers and cancer in the stomach in age groups (%)

The same tendency is observed between gastric ulcer and gastric cancer and even the frequency of encounter of gastric cancer with gastric ulcer overlaps in the 51-60 and ≥ 61 age groups. However, the chart shows that while peptic ulcer is seen in all age groups from the III decade, cancer is seen only from the V decade of age. DGR was detected in the case of 49.9% in women and 40.5% in men (p<0.01). Hp was found in 76.9% of men and 56% of women (p<0.05).
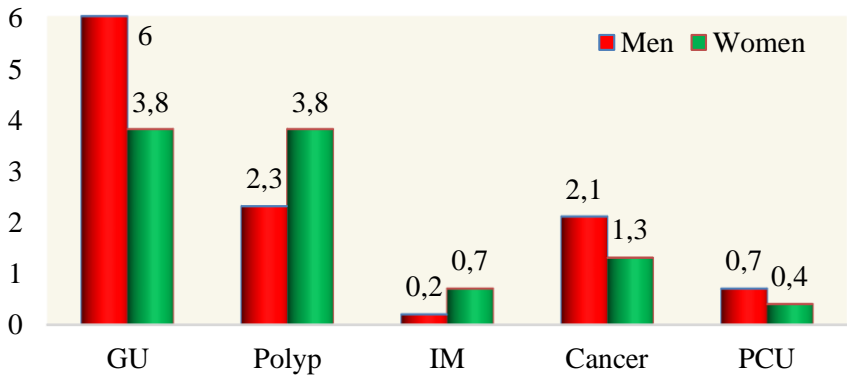
Chart 4. Frequency of occurrence (%) of gastric pathologies between 1-10% according to sex

Although pyloric canal ulcer, gastric ulcers, and gastric cancer were more common in men, and gastric polyps and intramural masses were more common in women, the difference was not statistically significant (p>0.05) (Chart 4).

The correlation between upper GIC and pathologies detected in the stomach

On endoscopic examination, those with high GIC have a very low odds of having a normal stomach (OR=0.22, inverse connection) and this is a statistically accurate ($p_1<0.05$) (Table 2).

Table 2

The correlation between gastric pathologies odds ratio (OR), complaints and outcome

Diagnosis	OR	Correlation	p_1	χ^2	p_2
Norm	0.22	Inverse	$< 0.05^*$	30.95	$< 0.001^{**}$
Erosive gastritis	3.76	Straight	$< 0.05^*$	10.37	$< 0.001^{**}$
DGR	3.54	Straight	$< 0.05^*$	14.04	$< 0.001^{**}$
PD	7.02	Straight	> 0.05	4.05	$= 0.044^{**}$

Notes: 1. p_1 * – compared to CG;

2. p_2 ** – the correlation between the complaint and the outcome.

There is a straight and reliable statistical correlation between erosive gastritis and upper GIC (OR=3.76; $p_1<0.05$), that is, complaints the likelihood of erosive gastritis in individuals with complaints is very high ($\chi^2=10.37$; $p_2<0.001$).

One of the gastric pathologies is duodenogastric reflux that having a statistically straight, accurate relationship with the upper GIC (OR=3.54; $p_1<0.05$; $\chi^2=14.04$; $p_2<0.001$).

There is an unreliable straight ratio between pyloric dysfunction and upper GIC, which is among the causes of DGR and is also found in patients in control groups (OR=7.02; $p_1>0.05$).However, in terms of complaint and endoscopic outcome, this correlation is statistically reliable ($\chi^2=4.05$; $p_2=0.044$).

Features of the correlation between extraoral halitosis and gastric pathology

When DGR, which we endoscopically detected in individuals with extraoral halitosis (group I) on the background of upper GIC, was compared only with group with GIC (group II), it was found that the relationship between DGR and extraoral halitosis is correct, statistically valid, and its statistical power is moderate (OR=12.6; χ^2=62.38; p<0.001; φ=0.242). From a clinical point of view, this gives the value of the prognostic criterion "in favor" for extraoral halitosis DGR.

The correlation between extraoral halitosis and Hp infection is inverse, valid, and has medium power (CR=0.27; χ^2=7.64; p<0.01; φ=0.267). The strongest statistical correlation we found during the research was found between group I and DGR seen in the stomachs of patients in CG (group III).

The correlation here is direct due to its characteristics, (OR=39.24), statistically significant, (χ^2=64.22 and p<0.001) and this correlation is very strong (φ = 0.717). Therefore, extraoral halitosis can be assessed as a prognostic criterion "in favor" of the DGR (Table 3).

Table 3

Features of the correlation between extraoral halitosis and gastric pathology

Comparison groups	Result	OR	Correlation	χ^2	p<	The power of correlation (φ)
I and II	DQR	12.6	Direct	62.38	0.001	0.242**
	Hp	0.27	Inverse	7.64	0.01	0.267**
I and III	DQR	39.2	Direct	64.22	0.001	0.717***
	PD	6.92	Direct	4.27	0.05	0.185*

Notes: * – the statistical correlation is weak; ** – is medium; *** – is strong.

The correlation between PD and extraoral halitosis observed in patients in CG during endoscopy is also direct, (OR= 6.92),

statistically significant,(χ^2 = 4.27 and p<0.05) and the power of this correlation is weak (φ = 0.185). This suggests that although PD plays a role in the extraoral causes of halitosis, the importance of DGR is very high.

Frequency of occurrence of the pathologies detected in the duodenum

Duodenoscopy was performed in 50 patients in CG and 1051 patients in PG. The mucosa and anatomical structure of the duodenum were endoscopically normal in 80.0% of patients in CG and 60.4% of patients in PG (p<0.05).

More than 10% of pathologies in the duodenum were erosive bulbitis - 19.1% and ulcers - 10.4%. The frequency of these pathologies in CG was 12% and 4%, respectively.

Pathologies with a frequency of 1% to 10% among patients include scar deformity of the duodenum - 4.9%, bulbitis - 3.2%, duodenitis - 5.7%, erosive duodenitis - 1.9% and polyps - 1.0%. Scar deformity of the bulbous was observed in 4.0% of those in CG, and duodenitis and polyps in 2%. (p>0.05).

Pathologies with a incidence of less than 1% in our patients in PG included celiac disease (0.3%), diffuse nodular change (0.1%) and diverticula (0.9%).

Results of histopathological examination of duodenum biopsies

During EGD, we performed a biopsy of the duodenal mucosa of only 9 patients for histopathological examination. Of these biopsies, 3 had duodenitis, 2 had mucosal hyperplasia, 2 had polypoid tissue, 1 had villous adenoma, and 1 had histopathological changes related to celiac disease.

Age and sex characteristics of duodenum pathologies

Normal appearance of the duodenum was found the most in the ≤ 20 (74.6%) and least in the 51-60 age group (52.35%; p<0.05). Erosive

bulbit and duodenal ulcer were the most common (23.6% and 13%) in the 41-50 age group and the least common (11.1% and 4.8%) in the 20, respectively. Bulbit was the most common pathology in the age group of 51-60 years (5.3%) and the least in ≤ 20 (1.6%). Celiac disease (1.2%) and diffuse nodular changes were observed only in the 31-40 age group (0.4%).

In general, taking into account the ratio of men to women, it is clear that duodenal pathology is 1.8 times more common in men than in women. In particular, the sex-dependent dependence of pathologies such as duodenitis, duodenal ulcer and erosive bulbitis is statistically correct ($p < 0.01$). Although celiac disease was more common in female patients than in male patients, the difference was not statistically significant ($p > 0.05$).

Features of the correlation between upper GIC and duodenal pathology

There is a correlation between the complaint and the endoscopic result, as the odds of the duodenum mucosa being normal are very low in those with upper GIC. (OR=0.38; $p_1 < 0.05$). In contrast, there is a statistically valid and straight correlation between upper GIC and duodenal pathology ($\chi^2 = 7.71$; $p_2 = 0.005$).

Compared to CG, those with upper GIC have a higher odds of developing duodenal ulcer disease (OR=2.78), duodenitis (OR=2.97) and bulbitis (OR=3.42), but this difference is not sufficient to be a prognostic criterion ($p_1 > 0.05$).

We did not find a statistically significant correlation between extraoral halitosis and duodenal pathology.

Frequency of occurrence of the pathologies detected during colonoscopy in the rectum

The most common pathologies of the rectum in PG were hemorrhoids (35.7%) and proctitis (10.8%). Although hemorrhoids were more common in CG (27.1), proctitis was found in only 4.2% of cases.

Pathologies with a prevalence of 1% to 10% in the rectum included rectal cancer (1.7%), anal fissure (4.1%), prolapse (1.7%), concomitant hemorrhoids and anal fissure (6.2%), and erosive proctitis (8.3%). In the PG we encountered rectal polyps in 9.5%, and in the CG in 12.5%.

During colonoscopy, endoscopic signs of Crohn's disease (0.7%) and ulcerative colitis (0.3%) were found in less than 1% of pathologies in the rectum.

Colonoscopy revealed no pathology in the rectum of 32.0% of patients in PG and 60.4% of patients in CG ($p<0.01$).

Characteristics of rectal pathologies according to age and sex

The difference between age groups in pathologies such as anal fissure, hemorrhoids, concomitant hemorrhoids and anal fissure, sudden prolapse, proctitis, and rectal ulcer was not statistically significant. The rectal symptoms of Crohn's disease and ulcerative colitis were found only in the 31-40 age group. Rectal polyps were most common in the IV, V, and VI decades of age (10.3-14%), and least in the ≤ 30 age group (1.9%) ($p<0.05$).

We have encountered colorectal cancer since the V decade of age (1.8%). In the VI decade of age, the disease was more common (4.2%) and was seen only in women.

Although polyps, rectal ulcers, erosive proctitis, sudden prolapse, and hemorrhoids were more common in male patients, and proctitis, anal fissures, and concomitant hemorrhoids and anal fissure were more common in women, the difference was not statistically significant ($p>0.05$).

Pathologies detected in the colon intestine

The pathologies we found in the colon intestine are given in Chart 5. The histogram in the figure shows that the most common pathology in the Sigmoid colon is erosive-ulcerative inflammation (44.2%). This chart, which is also high in the descending colon (37.2%), decreases to 9.3% in the transverse colon and the ascending colon. A similar

tendency applies to other types of inflammation (non-erosive ulcers) (respectively: 41.7%; 29.2%; 12.5% and 16.6%). As can be seen, inflammatory changes in the left half of the colon are generally very characteristic. The majority of colon polyps (35.5%) are located in the Sigmoid colon. 22.6% of polyps were found in the descending colon, 17.7% in the transverse colon, and 24.2% in the ascending colon.
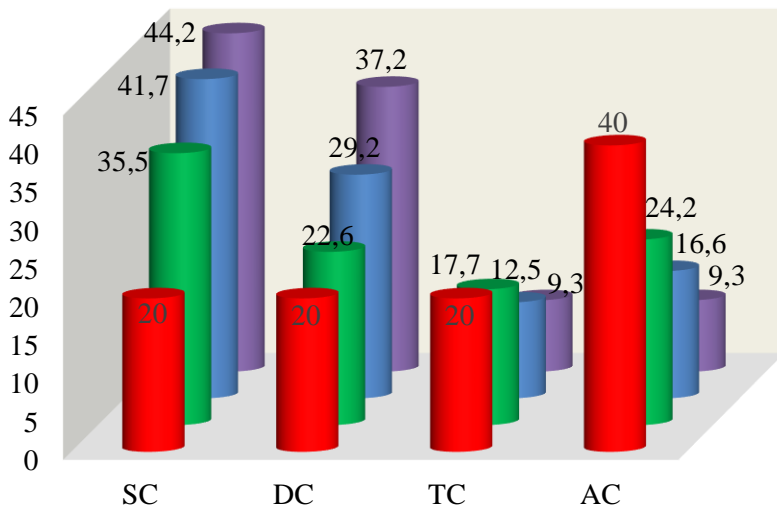
Notes: SC – Sigmoid colon, DC – Descending colon, TC – Transverse colon, AC – Ascending colon

Chart 5. Encounter proportion of pathologies in the colon intestine (%)

During the study, we found cancer in colon intestine of 5 patients.Depending on the location, cancer was seen in 2 patients with ascending colon (40%), in 1 of the remaining 3 patients in transverse colon (20%), in another in descending colon (20%), and in the third in Sigmoid colon (20%).

**Encounter frequency of colon pathologies by age and sex**

We grouped the pathologies we found under the names of cancer, polyps, anatomical changes (diverticula and angiodysplasia) and

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inflammatory changes (both erosive-ulcerative and other types of inflammation of the mucous membrane) (Chart 6).

This histogram shows that we did not encounter colon cancer in our patients under 51 years of age. Colon cancer was found in 1.4% of patients aged 51-60 years and in 13.3% of those in the ≥ 61 age group.

The polyps we found in the colon intestine were also strongly dependent on the age factor, thus, the polyp, which was 1.9% in the ≤30 age group, was multiplied several times in the following age groups (respectively: 6.7%; 25%; 37.7%; 53.3%).
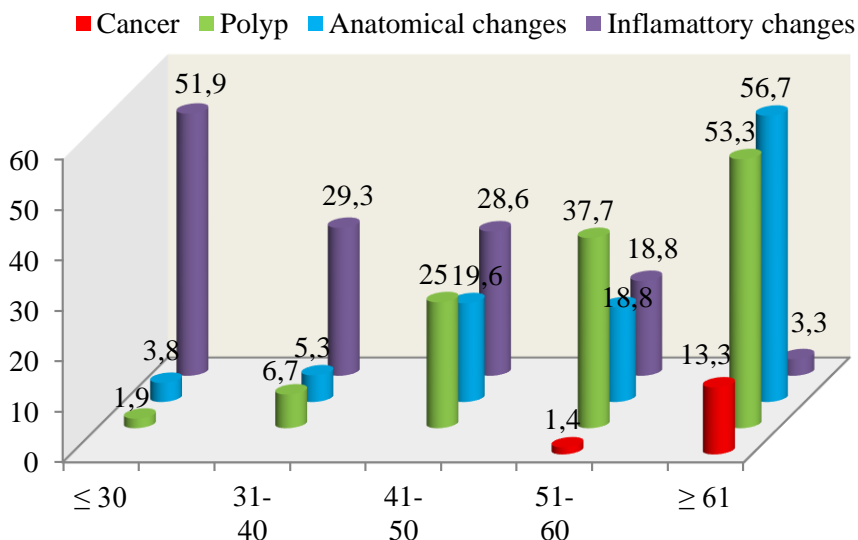
Chart 6. Proportion of colon pathologies in age groups (%)

The results of the study showed that the anatomical changes of the colon also depend on the age factor. Such pathologies were seen as 3.8% in the age group of ≤30, 5.3% in 31-40, 19.6% in 41-50, 18.8% in 51-60, and 56.7% in ≥61.

The exact opposite has been observed in inflammatory diseases of the colon intestine. Signs of inflammation in 51.9% of those in the ≤30 age group decreased to 29.3% in the IV decade of age, 28.6% in V, 18.8% in VI, and 3 in VII and 3.3% in the older.

We found that the Sigmoid colon and descending colon`s mucosa of female patients were in a normal state (75.4% and 85.9%) more than men (62.1% and 71.4%), respectively (p<0.05).

Melanosis choline and polyp, which we saw as at least 0.5% and at most 2.5%, was not dependent on the sexfactor.

We did not see diverticulitis, Crohn's disease and ulcerative colitis in men, and angiodysplasia in women. Inflammation of the mucous membrane of the colon intestine did not depend on gender.

By type, erosive-ulcerative inflammation was more common in the left half of the colon intestine in men (17.5%) than in women (5.2%) (p<0.05). We only found colon cancer in women.

Pathologies detected in the Cecum

No pathology was found in the cecum of 100% of people in CG and 89.8% of people in PG. The pathologies we identified consisted of melanosis coli (2.1%), erosive typhlitis (2.1%), typhlitis, Crohn's disease and polyps with 1.6% each, and lipoma, diverticulitis, and ulcer with 0.5% each.

Melanosis coli was found in all age groups (excluding 51-60 years) between 2.1% and 4.3%. Lipomas and polyps have been found since the sixth decade of age. No pathology of the appendix showed a statistically significant dependence on the sex factor.

Results of histopathological examination of colon biopsies

Colonoscopy revealed that 8.2% of the diagnostic biopsies from 61 patients showed lymphocytic inflammation, 18% had histopathological changes associated with Crohn's disease and ulcerative colitis, 6.6% had hyperplasia, and 9.8% had proliferation, 4.9% had metaplasia andthe same number had dysplasia and cancer (adeno-carcinoma).

57.4% of the biopsies were found that polyps we took from the lesion in the form of tumors. Of these, 5.5% were of inflammatory origin, 30.6% were hyperplastic, 55.6% were tubular adenoma, 5.5% were villous adenoma, and 2.8% were tubulo-villous adenoma.

Correlation between lower GIC and colon and rectal pathologies

To facilitate the interpretation of the correlation between lower gastrointestinal complaints and the pathologies detected by colonoscopy, we divided them into three groups:

1. Under the heading of anatomical changes anal fissures, hemorrhoids, concomitant hemorrhoids and anal fissure, prolapse, diverticula that we see in the rectum during colonoscopy;
2. Under the heading of inflammatory changes edema and hyperemia of the mucous membrane of the colon, erosive ulcer changes, Crohn's disease, ulcerative colitis and diverticulitis;
3. Tumors that are not aggravated, ie not inflamed, do not bleed and do not significantly narrow the intestinal tract (polyps, lipomas and cancer) combined under the heading of unaggravatedtumors.

The obtained data of the statistical processing of the research results are shown in Table 4. The study found that the anatomical changes found in the PG were greater than in the CG, and that the direct correlation between the lower GIC and the anatomical changes in the colon was statistically significant (OR=2.95; $p_1 < 0.05$).

The correlation between the complaint and the colonoscopic result is also significant ($\chi^2 = 4.27$; $p_2 < 0.001$).

From a clinical point of view, the meaning of these indicators is that patients with lower gastrointestinal complaints are more likely to experience any anatomical changes in the colon intestine, especially its distal part, during colonoscopy.

Table 4 also shows that people with low GIC are ten times more likely to have inflammatory bowel disease than CG.

There is also a statistically significant correlation between lower GIC and inflammation of the colon.

The correlation between the complaint and the colonoscopic result is also statistically significant (OR= 10.50; $p_1 < 0.05$; $\chi^2 = 5.56$; $p_2 < 0.001$).

Table 4
**Correlation between colorectal pathology odds ratio (OR),
lower GIC and colonoscopic outcome**

Pathology	OR	Correlation	p_1	χ^2	p_2
Anatomical changes	2.95	direct	< 0.05	4.27	<0.001
Inflammatory changes	10.59	direct	< 0.05	5.56	<0.001
Unaggravated tumors	0.83	weak inverse	> 0.05	0.09	>0.05

When the colon is treated as a whole organ it turns out that there is a weak inverse correlation between unaggravated tumors and low GIC detected during colonoscopy (OR=0.83; p_1>0.05). Here the relationship between the complaint and the result is not statistically significant (χ^2=0.09; p_2>0.05). The clinical meaning of this is that there is no correlation between unaggravated tumors (especially polyps and lipomas) and lower gastrointestinal complaints in the colon during colonoscopy. Unaggravated polyps during colonoscopy are found almost equally frequently in both the patient and the control groups.

FUNDINGS

1. Endoscopic examination of patients admitted to the clinic with a therapeutic profile with gastrointestinal complaints revealed:
   a) The incidence of esophageal cancer is 0.8%. This pathology, which occurs in 0.4% in the V decade, 1.2% in the VI, and 6.3% in the VII and older, is 3 times more common in men than in women[13];
   b) The incidence of gastric cancer is 1.8%, the disease is 1.6 times more common in men, increasing by 0.4% in the V decade, 5.2% in the VI, and 9.5% in the VII and older[13,15];
   c) The incidence of colorectal cancer is 3.7%, it increases to 1.8% in the V decade, 5.6% in the VI, and 12.9% in the VII and older[4,5,11].

2. Histomorphological examination of biopsies taken from malignant lesions of the mucous membrane on endoscopic examination allows to detect changes (keratosis, metaplasia with pathological regeneration, increased mitotic activity and varying degrees of dysplasia)related to the pre-cancerous stage in the esophagus - 13.0%; in the stomach - 33.3%; in the colon and rectum - in 19.4% of cases[4].

3. There is a statistically valid, straight and relatively strong ($p<0.001$; OR=265.71; $\varphi=0.426$) relationship between the "signs of anxiety" in the background of dyspepsia and the esophageal candidiasis and in pathologies such as ulcers, leiomyomas and cancer in the esophagus, there is a statistically valid, medium and straight correlation ($p<0.05$; $\varphi>0.2$ - <0.4 and in all cases CR>30.0) (criterion in favor)revealed by endoscopic examination.There is a statistically significant, weak correlation ($p<0.05$; $\varphi=0.142$ and OR=0.26) (criterion in favor)between the "signs of anxiety" in the background of dyspepsia and the normal condition of the mucous membrane of the esophagus[14].

4. Extraoral halitosis is foundin $6.9\pm0.6\%$ of appealed patients to the hospital with a therapeutic profile, and most often between the ages of 21 and 40 (54% in total). There is a statistically

valid, straightand strong correlation (p<0.001; OR=39.24 and φ=0.717) between this pathology and duodenogastric reflux.Referring to these indicators, we can say for the first time that duodenogastric reflux is one of the causes of extraoral halitosis[15].

5. According to histomorphological types the prevalence of 5.5% are of inflammatory origin, 30.6% are hyperplastic, 55.6% are tubular, 5.5% are villous, and 2.8% are tubulo-villous colorectal polypsin the patient (21.6%) and control (25.0%) groups was 0.864, indicating that it was clinically asymptomatic.The highest prevalence of colorectal polyps in different age groups is 3.71 times between the age group ≤ 30 years and the age group 31-40 years,and based on this indicator, it can be said that the most suitable period for the search for polyps and endoscopic ectomy for the prevention of colorectal cancer in our country - the fourth decade of age[4,11].

PRACTICAL RECOMMENDATIONS

1. Duodenogastric reflux should be ruled out or confirmed, including by conducting EGD examination to determine the correct treatment in people with bad breath independent of oral hygiene (extraoral halitosis).

2. Due to the fact that people with complaints of neoplastic formations of the tubular organs of the gastrointestinal tract, compared with the population of the country as a whole, esophageal cancer, stomach cancer, colon cancer is more common, it is necessary to recommend endoscopic examination to people with gastrointestinal complaints. In Azerbaijan, the most suitable age for screening of colon polyps is ≥ 31 years, and for cancer screening - ≥ 41 years.

3. In colonoscopy during chronic diarrhea, it is advisable 8-10 biopsies of the mucosa of various parts of the intestine to exclude microscopic colitis in persons with normal appearance of the mucous membrane of the colon intestine.

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LIST OF ABBREVIATIONS

CG   – control group
CRC   – colorectal cancer
DGR   – duodenogastric reпux
EG   – erosive gastritis
EGD   – esophago-gastro-duodenoscopy
EHD   – esophageal hernia of the diaphragm (hiatal hernia)
GERD   – gastro-esophageal reflux disease
GIC   – gastrointestinal complaints
GU   – gastric ulcers
IM   – intramural masses
PCU   – pyloric canal ulcer
PD   – pyloric dysfunction
PG   – patients group
OR   – odds ratio

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