MEDICAL SCIENCE

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DISCOVERY
SCIENTIFIC SOCIETY

Medical and social characteristics of the main risk factors of the development of gastric cancer in conditions of stress

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ABSTRACT

Background: Socio-economic and socio-psychological factors associated with the malignancy of precancerous diseases in malignant neoplasms of the stomach negatively affect the material well-being and social activity of patients, limit their life activities due to deterioration of physical and psychological well-being, lead to dissatisfaction with the state of health and to complaints of constant distress against the background of increased value of life itself. *Methods:* An analytical retrospective epidemiological medical-sociological study of a representative number of patients with gastric malignancies - 130 patients from the leading group and 50 people with precancerous diseases of the stomach from the comparison group - was conducted with the aim an in-depth study of medical and organizational risk factors in the study. *Results:* Risk factors for malignant transformation of gastric precancerous disease were found to be mostly modified, in addition to uncontrolled: behavioral - unfavorable eating habits: Too frequent meals (OR=5.27; 95% CI=2.59-10.72), excessive intake of sweet foods(3.48; 1.28-9.48), caffeinated beverages (3.37; 1.64-6.92) and alcohol (3.12; 1.44-6.78), insufficient fluid intake (3.04; 1.43-6.45), smoking (2.97; 1.46-6.06), especially intensive (5.80; 1.10-30.50), occupational-industrial hazards of chemical nature and contact (2.30; 1.02-4.20), genetic -hereditary amnesia (5.20; 2.25-12.02) and social - living in rural areas (28.61; 8.44-97.03). Gastrointestinal discomfort (2.93; 1.39-6.18) and weight loss (2.07; 1.07-4.02) were established to be predictors of malignant transformation. *Conclusion:* The appearance of new malignant neoplasms of the stomach is due to both uncontrollable risk factors and, in the vast majority, modified ones, and stressful situations contribute to the slightest degree of malignancy of precancerous gastric diseases.

Keywords: Gastric cancer, precancerous diseases of the gastric, risk factors, stressful situations

1. INTRODUCTION

Malignant neoplasms (MNS) today remain one of the most critical healthcare problems both in the world and in Ukraine (Titova, 2018). Its relevance is due to the constant increase in the incidence of this pathology in the population, the difficulty of timely diagnosis, the high cost and difficulty of treatment, and the high level of disability and mortality of patients (Shafransky et al., 2016). Our knowledge of cancer today is greater than ever before, which will undoubtedly help humanity make tremendous progress in the fight against it. By reducing the impact of harmful carcinogenic risk factors and increasing the effectiveness of cancer prevention measures, we can improve the diagnosis and treatment of this disease. A thoughtful approach and access to health care can save millions of lives. By improving social and political skills, the medical community seeks to dispel misconceptions about cancer and change behaviors and attitudes toward lifestyle, a major cause of cancer.

Since the beginning of the Russian invasion of Ukraine on February 24, 2022, 44 attacks on Ukrainian medical facilities have been recorded. The greatest fears are caused by these destructions, which occurred shortly after the COVID-19 pandemic, and will have serious short-term and long-term consequences, threatening Ukraine's lagging behind global scientific and technological progress. That is why the European Union provides unprecedented humanitarian aid to our country, which has been leading war for independence. It is quite realistic to believe that soon the impact of the war will go beyond the borders of Ukraine and may lead to an increase in the incidence of cancer not only in our country, but also in other countries. These risks are genuine, as numerous wartime carcinogens and toxins can spread over long distances from the battlefields, affect the environment and human health, pollute the air, soil, and water in the cities, and damage agricultural lands of Ukraine.

Gastric cancer occupies an essential place in the gastrointestinal tract, which remains one of the most common and deadly neoplasms worldwide. The incidence of malignant neoplasms of the gastric (GMN) ranks fifth among all cancers (5.7% of all new cancer cases) and ranks second in the structure of cancer incidence of digestive organs (Balakrishnan et al., 2017; Smyth et al., 2020). In particular, in economically developed countries, the specific weight of malignant neoplasms of the stomach reaches 50% of all tumors of the gastrointestinal tract and 10-15% of all malignant neoplasms (Thrift and Nguyen, 2021; Bray et al., 2018). Every year, more than a million new cases of GMN have to diagnose worldwide, and more than 600,000 people die from it, despite the stabilization of the incidence in some developed countries (Jung et al., 2019; Lyons et al., 2019). According to the Global Cancer Observatory, GMN is the third leading cause of death from cancer worldwide, after total mortality from lung cancer and colorectal cancer.

Approximately 1 out of 12 of all deaths from oncology are due to GMN (Sung et al., 2021). High rates of death from gastric cancer are characteristic of most countries of Eastern Europe, while the lowest rates are recorded in the USA, Canada, New Zealand, as well as in the countries of Western and Northern Europe. This picture is primarily explained by the high average 5-year survival of patients with GMN in economically developed countries: in Western Europe - 18%, in the USA - 21%, and the highest - 53%, recorded in Japan as a result of mass screening in this country. In the world, in general, the 5-year survival rate from GMN ranges from 10 to 20% (Van-Kleef et al., 2021). Ukraine ranks 8-9 among 49 countries with recorded cancer incidence. Every year in Ukraine, 6-8 thousand new cases of GMN are reported (among men - 22.3 per 100 thousand population, women - 12.6%ooo) (Fedorenko, 2022).

Science today knows hundreds of reasons that increase the risk of developing malignant pathology. There is reliable information that the specific weight of nutrition in the development of cancer is from 30 to 40%, smoking 40-50%, infectious agents - from 10 to 20%, alcohol consumption - 5-10%, environmental factor 5%, burdened heredity 5%. At the same time, it is impossible to evaluate each of these reasons separately; it is even more difficult to determine it in each specific case of oncological pathology. At the moment, the fact remains undeniable that in most cases, the development of cancer is related to our lifestyle. It's important for people to understand the causes and symptoms of this disease, which may lead to oncology in the future. There are many reasons; here are the main ones:

Infection of the body with Helicobacter pylori bacteria;

Improper nutrition;

Smoking;

Strong alcohol;

Epstein-Barr virus;

Genetic factors;

Constant stress and anxiety;

Precancerous conditions (adenomatous polyps, chronic atrophic gastritis, peptic ulcer disease, Ménetrie's disease, B12 deficiency anemia), etc.

Numerous studies and researchers Abrahami et al., (2022), Brown et al., (2018) confirm the importance of endogenous and exogenous factors in the occurrence of stomach cancer. But, in our opinion, today, it is necessary to consider another important factor in the development of cancer - wartime carcinogens. The greatest risk to public health during and after war is soil damage. During the destruction of buildings, a significant amount of smoke, asbestos, sand, dust, solid particles and other carcinogens are released into the atmosphere, which leads to chemical pollution of soils and water bodies.

Powerful explosions can destroy the waterproof layer of bedrock, which will contribute to the ingress of toxin-contaminated water and organic substances into the soil. Aggressive pollutants seeped into aquifers (including the carcinogenic perchlorate used in munitions production) can be transported far beyond the battlefield. There is a danger that due to the decline of the economy and the health sector and the absence of state programs for prevention and cancer screening, the situation may worsen than it was in the pre-war period. The invasion of Ukraine by the Russian Federation may lead to higher incidence and mortality from cancer than would be the case in peacetime.

2. MATERIALS AND METHODS

In order to study environmental factors and identify potential risk factors for the development of malignant neoplasms of the stomach among the population of Chernivtsi region during 2019-2022, an analytical retrospective epidemiological medico-sociological study of a representative number of patients with gastric cancer (GC) - 130 patients of the Chernivtsi Regional Clinical Oncology Hospital were conducted dispensary (leading group). For the in-depth study of medical and organizational risk factors, 50 people with precancerous diseases of the stomach (PDG) - patients of the gastroenterology department of the city clinical hospital No. 3 in Chernivtsi (comparison group) were included. This made it possible to conduct research in the same conditions of providing medical care and, accordingly, identify specific pre-hospital risk factors for malignancy of a medical and organizational nature.

Among the interviewees, the share of men, regardless of the observation group ($p > 0.05$), was 63.3±3.6%, and women – 36.7±3.6%, corresponding to the known gender characteristics of stomach cancer incidence. The average age of respondents with stomach cancer was 60.0±0.9 years and among the comparison group - 56.6±0.9 years ($p < 0.01$). A total of 130 such persons (the leading group of the study), patients of the regional oncology dispensary, were examined, which ensured the sample's representativeness. To identify the risk factors of malignant neoplasms of the stomach, it was necessary to form a comparison (control) group. Therefore, according to the same program, 50 patients with precancerous diseases of the stomach were interviewed. By sex, the comparison groups (primary and control) did not differ from each other ($p > 0.05$). However, according to the age distribution, patients with malignant neoplasms of the stomach quite logically turned out to be somewhat "older" - 54.6% were over 60 years old against 36.0% of patients with precancerous diseases of the stomach ($p < 0.01$).

The comparison groups also differed significantly in terms of place of residence: the majority of interviewed patients with stomach cancer were residents of villages (64.6%) and patients with precancerous diseases of the stomach were residents of cities (94.0%, $p < 0.001$). The development and summarization of the material was carried out by grouping the received data according to the studied contingents (patients with stomach cancer and precancerous diseases of the stomach), place of residence (urban, rural residents), gender (men, women) and age (under 30 years, 30-34, 35 -39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75 years and older) and creating relevant databases based on Microsoft Excel. Statistical processing of the obtained data was carried out by calculating the frequency of distribution of factors per 100 respondents and error (±m) for relative values according to the well-known formula (Forthofer et al., 2007).

3. RESULTS

The study of the prevalence and intensity of harmful habits showed that such a well-known risk factor for GC as smoking was more common for the leading group (Figure 1). Only less than half of the respondents with gastric cancer have never smoked - 45.7±4.4% versus 71.4±6.5% in the comparison group ($p < 0.01$). The rest smoked (37.0% vs. 20.4%) or had this bad habit in the anamnesis (17.3% vs. 8.2%). The highest prevalence of smoking is among young (up to 45 years) patients with GMN - 82.5% ($p < 0.05$), and the share of those who quit smoking continues to increase and decreases slightly - those who continue to do so. Smoking is prevalent among men: 80.7% of the primary and 44.8% of the control group against 4.6-5.0% of women ($p < 0.001$). This bad habit was somewhat more common among patients with GMN among residents of villages - 59.3% compared to 45.7% of urban residents ($p < 0.05$).

Alcohol consumption was quite common among patients with GMN (Figure 1). In comparison with the group of respondents with PDG (p<0.05), there were significantly more people who drink alcohol 1-2 times a month (31.55 vs. 20.0%, respectively) or 1-2 times a week in the leading group (12.3% against 0%), that is, abuses it. On the contrary, there are significantly fewer people who do not drink alcohol at all or drink it less than once a month (56.2% versus 80.0%). Moreover, the respondents of the leading group usually preferred strong alcoholic beverages - 88.9% versus 41.2% (p<0.05). Again, the use of alcohol is more typical for men (p<0.001), among whom 60.7% in the leading group and 30.0% in the control group consumed it 1-2 times a month or more often compared to 11.1% and 5.0 %, respectively, which corresponds to the data of other studies.

As you know, eating habits, including water consumption, are an essential health factor. The most of respondents in our study preferred raw water (90.8% of the leading and 84.0% of the comparison group, p>0.05) and only 9.2% and 16.0% - boiled water. Residents of cities used boiled water more often (p<0.05). An important factor was the amount of water used per day (Figure 1). Almost half of the interviewees from the leading group (46.2%) consumed less than one liter of water, which is twice as much as in the comparison group (22.0%, p<0.05). On the other hand, the specific weight of those who consume the recommended daily amount of water (at least 1.5 liters) in the leading group is inferior to that in the comparison group - 26.2% versus 36.0%.

Regarding the mode and frequency of meals, only 6.9% of the respondents of the leading group and one person from the control group eat 1-2 times a day. The largest share in both groups, slightly higher in the control group, was those who prefer three meals a day (50.0% and 61.7%, respectively). Another third of respondents eat 4-5 times daily (27.7% and 34.0%). There is a significant difference in the specific weight of those who eat very often (more than five times a day): in the group of patients with GMN, 15.4% of them are against one respondent of the control group (p<0.05). That is, excessive load on the digestive system, in particular, too frequent meals, increases the chances of malignancy of the PDG (OR=8.36; 95%CI=1.09-64.17; p<0.05).

Regarding the consumption of unhealthy food, the study also found no significant difference between the comparison groups in the frequency of consumption of spicy, salty, fatty food / fast food and sweet carbonated drinks (p>0.05). It's encouraging that the aforementioned unhealthy food is consumed by a limited number of respondents. In particular, salty food is constantly consumed by 21.1±3.0% of respondents, spicy - 13.1±2.5%, sweet carbonated drinks - 11.7±2.4%, fast food - 7.4±2.0 %. These gastronomic preferences mainly concern men, because 28.6% of them against 6.5% of women (p<0.01) constantly consume salty food, 20.7% against 2.2% (p <0.05) – spicy, 14.3% vs. 4.3% (p<0.01) – sweet carbonated drinks and 9.8% vs. 0% (p<0.05) – fatty food.

Hypodynamia is a significant potential risk factor for chronic diseases. More than 60% of respondents (61.6±3.7%), regardless of health status, age, gender and place of residence (p>0.05), noted that they do not exercise at all (running, walking, gym, etc.). Of the rest, every fourth (26.6±3.3%) respondent indicated that they deal with them sporadically and only 11.9±2.4% - systematically. It was found that half of the surveyed patients with gastric cancer (51.6±4.5%) also had diseases of the digestive organs in the family (Figure 1). At the same time, in the comparison group, there were only 10.6± 4.5% and another 6.4% said they do not know (p<0.001). Other researchers point to the importance of family history. Our research confirmed that the importance of family anamnesis depends on the age of the respondents, as well as on the accumulated life experience (p<0.05), because the indicators standardized by age structure already differed significantly less from each other (52.2% and 40.6%).

GC patients indicated the presence of occupational hazards during their work twice as often as respondents from the control group: 37.7±4.4% versus 20.8±5.9%, respectively (p<0.05). But we note that if the comparison groups were standardized by age, there would be no difference in the frequency of this feature. That is, it can be assumed that with age, and therefore with the accumulation of work experience, the probability of harmful production factors in the professional route also increases. However, the study did not establish a difference in the duration of exposure to industrial hazards in the compared groups (p>0.05): Among those who noted their presence, 73.9% of the leading group and 70.0% of the control group were exposed to them for more than ten years.

The influence of stress on carcinogenesis is known due to activation of the sympathetic nervous system, inflammatory response, and suppression of cellular immunity, as well as changes in behavior and the acquisition of harmful habits that lead to the development of cancer (smoking, overeating, and drinking alcohol). The connection between psychological war trauma and cancer is of increasingly concerning to the medical community. In our study, patients with PDG were more likely to complain about severe psycho-emotional stress at work, which was also reflected in the fact that among them, the share of those who assessed the social and psychological climate in the work team as completely comfortable was 1.5 times smaller (26.2% versus 42.3% among patients with ZNS, p<0.05). Most of them (71.4%) and more than half of the respondents of the leading group (56.1%, p>0.05) rated relations with work colleagues as satisfactory, even in isolated cases (2.4% and 1.6%) - as unsatisfactory.
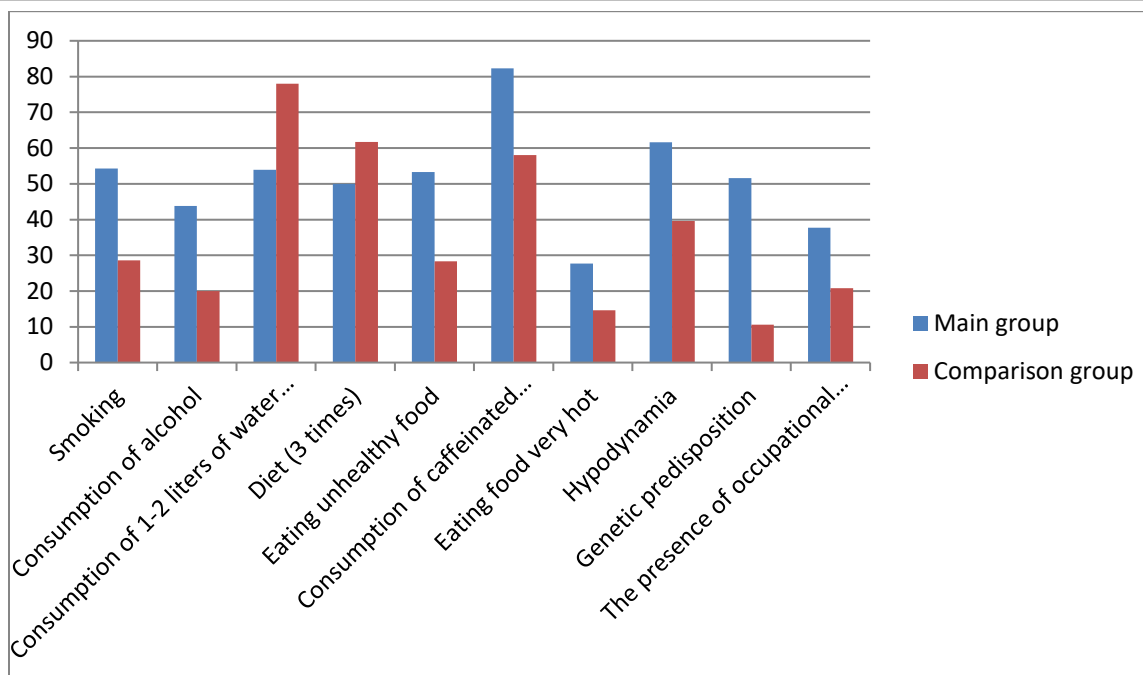
Figure 1 Distribution of respondents of the leading and comparison groups according to the principal causes of gastric cancer

As shown in Figure 2, the presence of constant stress was more often complained of by the interviewed patients with GC - 44.6±4.4% versus 28.0±6.3% in the control group (p<0.05). It is known that anxiety and distress are essential components of the deterioration of the quality of life, which decreases with the onset of such a severe, often fatal disease as GC, which was once again proven by our (OR=2.07; 95%CI=1.02-4.20; p<0.05) and other studies.
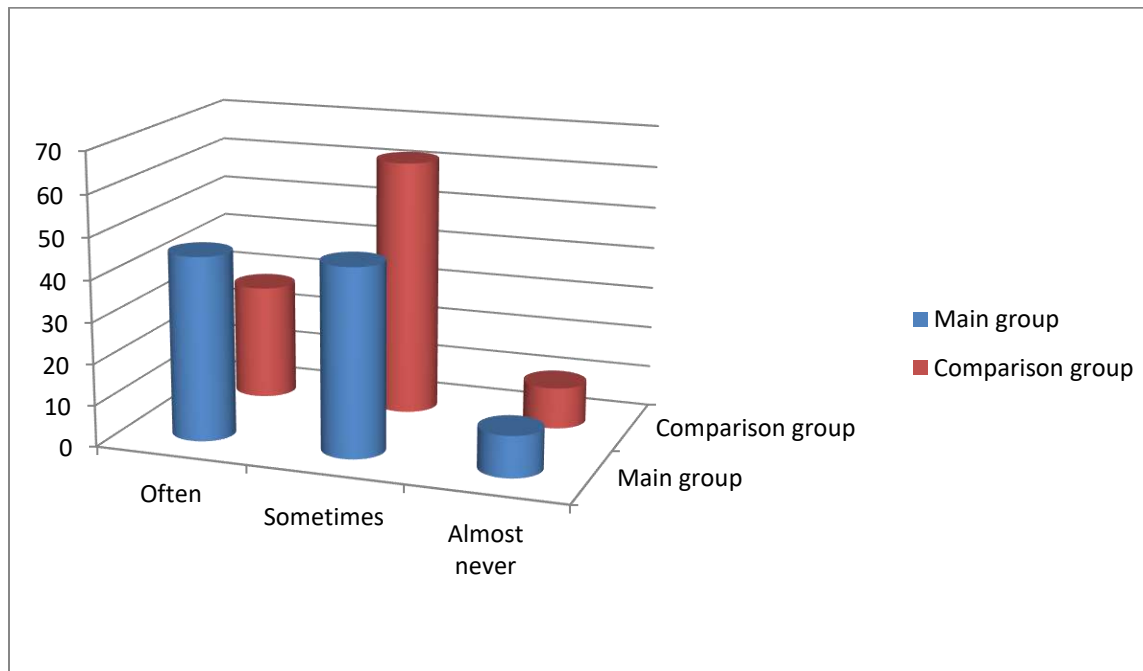

Figure 2 Distribution of respondents of the comparison groups according to the frequency of stressful situations in their lives (self-assessment data)

There is a danger that due to the decline of the economy and the health sector and the absence of state programs for prevention and cancer screening, the situation may worsen than it was in the pre-war period. An invasion of Ukraine by the Russian Federation may result in more disease and cancer deaths than would be expected in peacetime. Half of the interviewees from the leading group (54.0%) and the majority from the control group (81.2%) considered it satisfactory. It is reasonably expected that such

a disease as GMN increases the chances of complaints about an unsatisfactory state of health (OR=2.89; 95%CI=1.20-7.00; p<0.01), and accordingly, in the leading group, it was recorded twice more such answers than in the control group - 32.5% versus 14.3%. On the other hand, surprisingly, in the leading group, about 13% of respondents, much more often than in the comparison group, considered their health good (12.7% vs. 4.1%, respectively) and even excellent (0, 8% versus 0%).
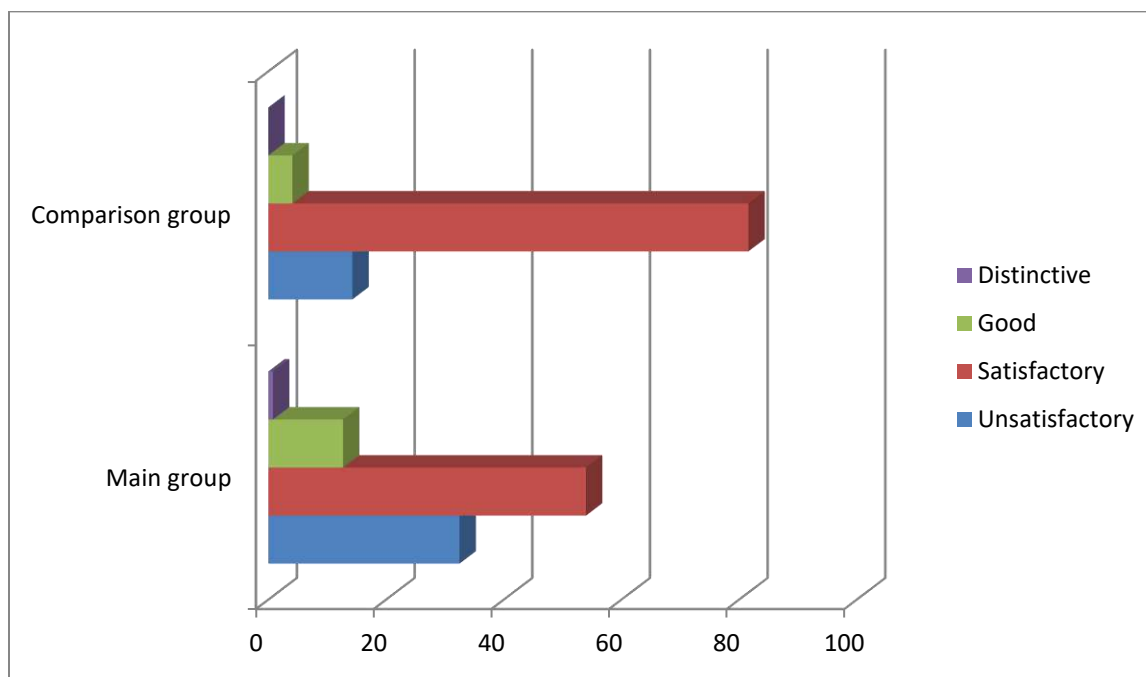

Figure 3 Results of the respondents' assessment of their state of health

In the same way, quite paradoxically, the respondents from GMN assessed their level of satisfaction with life (Figure 3). In particular, respondents in the leading group chose the answer "completely satisfied" twice as often as in the comparison group - 69.5% versus 34.7% (p<0.001). Obviously, with the appearance of a potentially fatal disease, the value of each lived day increases, and accordingly, the chances of greater life satisfaction (OR=4.30; 95%CI=2.14-8.64; p<0.001).

4. DISCUSSION

One of the known causes of stomach cancer is smoking (Ladeiras-Lopes et al., 2008). A systematic review of studies on the relationship between cigarette smoking and gastric cancer provides strong evidence that smoking is the most important behavioral risk factor for gastric cancer. Of the 72 case-control studies we found that examined the association between cigarette smoking and gastric cancer (Cai et al., 2003). Forty studies, observed a significant increase in risk among current smokers or subjects who had ever smoked compared with subjects who had never smoked (Minami and Tateno, 2003). Of 15 prospective cohort studies, Brenner et al., (2002), 10 studies observed a significant increase in risk among are smokers compared to those who have never smoked. Gastric cancer studies have reported conflicting results, with EUR says finding no positive association. In contrast, most and EMR studies show a higher risk of gastric cancer with smoking as well as the use of various types of e-cigarettes. However, a previous meta-analysis of Indian studies did not find a significant positive association between gastric cancer and e-cigarette use (1.31, 95% CI 0.92-1.87) (Sinha et al., 2016).

The results of our study are consistent with 40 case-control studies and 10 cohort studies, where nearly half of respondents, 54.3% of gastric cancer patients, are current smokers or have smoked in the past. A joint pooled analysis by the StoP Project Consortium found an association between heavy drinking (>4 drinks per day, approximately 50 g of ethanol per day) and gastric cancer risk. The risk was significantly increased (by about 50%) for those who drank six or more daily drinks (Praud et al., 2018). There is also relevant evidence of a link between heavy alcohol consumption and the risk of stomach cancer (Ma et al., 2015; Bagnardi et al., 2015). The meta-analysis by Tramacere et al., (2012) – based on 15 cohort and 44 case–control studies – found a 20% increased risk of gastric cancer (RR 1.20, 95% CI 1.01–1.44) for four or more alcoholic drinks per day, which also corresponds to our results. Still, it was not possible to investigate the role of high doses of alcohol, nor the effect of specific drinks.

A large population-based case-control study conducted in the United States found that the higher the intake of meat, especially poultry and full-fat dairy products, the higher the risk of gastric adenocarcinoma. Therefore, various modifiable and non-modifiable factors modulate the risk of gastric cancer, and it is crucial to consider these risks in the future to develop of new screening methods. Remember that diet, smoking, and alcohol consumption are essential risk factors for gastric cancer, but these can be changed. We would also like to point out that our study focused on risk factors such as drinking and eating habits, consumption of caffeinated beverages and very hot foods associated with gastric cancer, which have not been considered by other researchers, but may somehow have some influence on the development of gastric cancer. If we turn to the scientific point of view, there is no consensus among scientists the impact of stress on the development of tumors today.

Various studies (both statistical on large samples of patients and laboratory on animals) often show opposite results, which does not allow for an unequivocal answer, but will enable us to draw some conclusions. In our study, almost half of the respondents (44.6%) of the leading group were almost constantly in a state of stress, compared to 28.0% of the control group, which will inevitably lead to deterioration in the quality of life of patients and, accordingly, a further decrease in the body's defenses. Many people who experience long-term stress begin to lead an unhealthy lifestyle: they overeat, abuse alcohol, start smoking or smoke more than usual, sleep worse, and move less. Thus, stress indirectly contributes to the emergence of factors that provoke cancer.

5. CONCLUSION

Therefore, the degree of influence of stress on the risk of malignant neoplasms of the gastric is greatly exaggerated in the mass consciousness. Socioeconomic, socio-psychological, and behavioral risk factors proved to be much more essential. For example, smoking, especially heavy smoking, alcohol consumption, too frequent meals, weight gain, excessive consumption of sweetened and caffeinated beverages, inadequate fluid intake, lack of adequate rest at home, and work activities associated with industrial risk factors. It is possible to make long-term predictions about the development of cancer in Ukraine after the end of hostilities only based on the experience of countries that have previously fought wars - Vietnam, Iraq, Afghanistan, Syria, and the Balkan countries.

Author Contributions

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

Ethical approval

The study acquired the ethical approval from the Commission on Biomedical Ethics for compliance with moral and legal rules of medical research of Bukovynian State Medical University of the Ministry of Health of Ukraine, (letter number Nr. 2 from 18.02.2021 - project number 0120U102625).

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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