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OBESITY – AN ELEMENT OF METABOLIC SYNDROME

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Mihaela Ionela VLADU²
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ABSTRACT:

METABOLIC SYNDROME (MS) IS DEFINED BY LOW TOLERANCE TO GLUCOSE, DYSLIPIDEMIA, HYPERTENSION, OBESITY AND HYPERINSULINEMIA. THROUGH ALL OF THESE FACTORS MS FAVORS INCREASED CARDIOVASCULAR RISK, WHICH IS WHY IT SHOULD BE DETECTED EARLY. ALTHOUGH THESE FACTORS IN THE MS HAVE BEEN KNOWN FOR SOME TIME, THE MOST IMPORTANT IS INSULIN RESISTANCE. DUE TO INSULIN RESISTANCE, PEOPLE WITH MS HAVE A HIGH RISK OF MORTALITY DUE TO CORONARY ARTERY DISEASE.

THE CONCEPT OF MS IS AN OPEN WINDOW TO RESEARCH, A CONCEPT OPEN TO THE NEW, AN IMPORTANT TOPIC OF DEBATE IN TERMS OF ITS SPREADING AREA AND THE EVER-INCREASING GLOBAL INCIDENCE.

THE FIRST EPIDEMIOLOGICAL STUDY OF THE PREVALENCE OF OBESITY AND RISK FACTORS FOR OBESITY IN THE ADULT POPULATION IN ROMANIA WAS PUBLISHED IN 2015 AND ESTIMATED THAT 21.3% OF ROMANIANS AGED OVER 18 YEARS SUFFER FROM OBESITY.

THE TOPIC ADDRESSED IN THIS PAPER BELONGS TO A PRIORITY AREA OF PUBLIC HEALTH IN THE EUROPEAN UNION AND ROMANIA. THE MAIN PURPOSE OF THIS WORK WAS TO ANALYZE THE ASSOCIATION OF OBESITY WITH OTHER CHRONIC CONDITIONS SUCH AS: T2DM, HYPERTENSION, HYPERCHOLESTEROLEMIA, HYPERTRIGLYCERIDEMIA, DYSLIPIDEMIA, LIVER STEATOSIS, BILIARY LITHIASIS.

KEY WORDS: HYPERTENSION, METABOLIC SYNDROME, DYSLIPIDEMIA, OBESITY

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INTRODUCTION

Metabolic syndrome (MS) is defined by low tolerance to glucose, dyslipidemia, hypertension, obesity and hyperinsulinemia. Through all of these factors MS favors increased cardiovascular risk, which is why it should be detected early. Although these factors in the MS have been known for some time, the most important is insulin resistance. Due to insulin resistance, people with MS have a high risk of mortality due to coronary artery disease.

The clinical identification of MS is based on the evaluation of abdominal obesity, dyslipidemia, hypertension and glucose intolerance. Among the essential criteria of the MS, according to the WHO, insulin resistance and the estimation of insulin consumption or its substitutes play an important role.

The US National Program for Cholesterol Education proposes a more streamlined definition for clinical practice, but does not include insulin resistance. Thus, people with MS must meet three of the following criteria:

- high blood pressure (> 130 / 85mmHg)
- high plasma glucose (> 110 mg / dl)
- abdominal obesity (abdominal circumference > 102 cm in males and > 88 cm in women)
- low serum HDL-cholesterol (< 40 mg/dl in men and < 50 mg/dl in women)
- elevated serum triglyceride levels (> 150 mg /dl).

The International Diabetes Federation (IDF) proposes an essential criterion for defining the MS, which is the central obesity, the values of the abdominal circumference varying within certain limits according to the characteristics of the ethnic groups of the evaluated persons. Identifying patients with MS is a practical and extremely useful way of screening patients who have multiple risk factors that predispose them to diabetes and cardiovascular disease.

The prevalence of MS in developed countries is among adult adults at around 22-39%, this percentage varying according to the criteria included in its definition. The MS is associated with future coronary events and type 2 diabetes mellitus (T2DM).

The concept of MS is an open window to research, a concept open to the new, an important topic of debate in terms of its spreading area and the ever-increasing global incidence.

The first epidemiological study of the prevalence of obesity and risk factors for obesity in the adult population in Romania was published in 2015 and estimated that 21.3% of Romanians aged over 18 years suffer from obesity.

The topic addressed in this paper belongs to a priority area of public health in the European Union and Romania. The main purpose of this work was to analyze the association of obesity with other chronic conditions such as: T2DM, hypertension, hypercholesterolemia, hypertriglyceridemia, dyslipidemia, liver steatosis, biliary lithiasis.

MATERIAL AND METHODS

The study was conducted on a group of 110 patients with different degrees of obesity admitted to the Medical Clinic II and the Department of Diabetes Nutrition and Metabolic Diseases of the Municipal Clinical Hospital of Filantropia Craiova over a period of 15 months (January 2016 - March 2017). The study was retrospective, all the data being analyzed, being extracted from the clinical observation sheets prepared for each patient admitted to the health unit.

Reasons for hospitalization were varied, mostly in relation to cardiovascular pathology (especially hypertension), metabolic syndrome and unbalanced T2DM.

The major criterion for inclusion in the study was obesity regardless of its degree. The first data retained from the clinical observation sheets were those of a general nature: the age of the patients; sex; the residence environment. Thus, patients were divided into age groups (40-49 years, 50-59 years, 60-69 years) by gender (male / female) and by country of origin (rural / urban).

The data about the height and weight of each patient were used to calculate the body mass index, according to the formula: $IMC = \text{weight (kg)} : \text{height}^2 \text{ (m)}$

The nutritional status of each patient was assessed and their classification was made according to the degree of obesity:

- grade I obesity with BMI in the range 30-34.9 kg / m²
- grade II obesity with BMI in the range 35-39.9 kg / m²
- grade III obesity (morbid) with BMI > 40 kg / m²

Data on abdominal circumference values for the assessment of central / visceral obesity was extracted and analyzed. The baseline values for the current study were: ≥ 94 cm for men and ≥ 80 cm for females.

Both study groups, female and male were divided into subcategories in agreement with abdominal circumference (AC) values:

- for women: 80-84.9 cm; 85-89.9 cm; 90-94.9 cm; 95-99.9 cm; and > 100 cm
- for men: 94-99.9 cm; 100-104.9 cm; 105-109.9 cm; 110-114.9 cm and > 115 cm.

Next, I extracted anamnestic data on the existence of risk behaviors for obesity, hypertension and T2DM.

I have emphasized on food appreciation, smoking assessment, physical activity assessment (assessment of sedentary status).

Paraclinical laboratory data such as the values of the lipid profile (total cholesterol, HDL cholesterol, triglycerides), and blood glucose values were also retained. For each of these, the minimum, maximum, average values and the standard deviation were calculated.

We wanted to identify cases with hypercholesterolemia (> 200 mg/dl), hypertriglyceridemia (> 150 mg/dl) and mixed dyslipidaemia (elevated total cholesterol and triglycerides and diminished HDL cholesterol).

At the same time, the tension values were analyzed for each case, the aim being to estimate the prevalence of hypertension in obese patients. The cases already known with high blood pressure and with values kept under control by specific therapy were also retained.

Starting from the notion that obesity and insulin-resistance imply heavy hepatocyte loading, the study aims to evaluate the prevalence of hepatosteatosis in obese patients. Thus, from the data provided by the imaging investigations, we used the ultrasound assessments performed in the liver and the cholecysterase and we noted the cases with hepatic steatosis and gallstones. The status of liver steatosis was assessed for each case as being: absent, mild, moderate or severe. The liver with normal characteristics in terms of size, ecostation and homogeneity was considered devoid of hepatic steatosis. We considered the steatosis liver to be of a size above normal range and a hyperecogenic aspect compared to renal cortical, "brilliant", accompanied by posterior mitigation due to partial absorption of ultrasound by fatty tissue.

After data collection, dates were centralized statistically, being coded according to the studied variable. Once data encoding has been completed, they were entered into a database created

in Office Excel, and the statistical analysis was performed using the SPSS 17 computer assisted program.

RESULTS

The study group comprised a total of 110 known patients with obesity of varying degrees, regardless of the subjective accusations for which they were admitted.

Of the total patient population, 67 were women and 43 men. Percentually, the female group accounted for 61% and the male 39%.

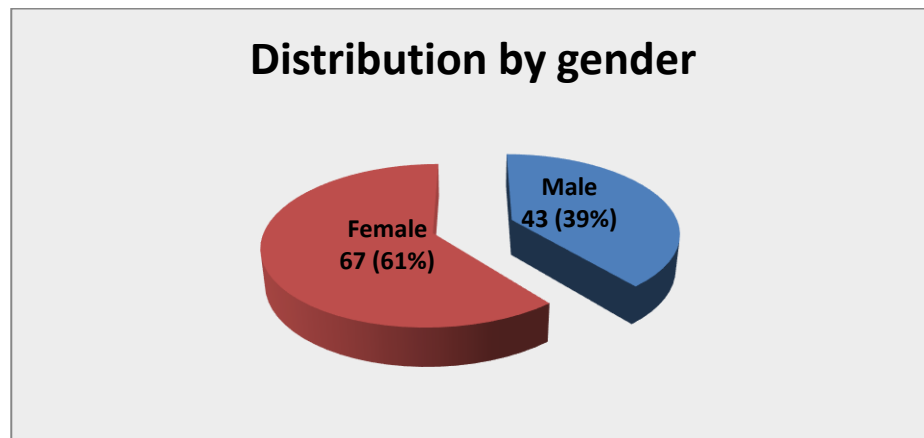


Figure 1. Distribution of cases by gender

In the general study group, 26 cases were rural (23.6%) and 84 urban (76.4%). The place of origin was studied for both the female and the male group.

Thus, in the women group, 17 cases came from the rural area and 50 from the urban area, while in the male group, 9 cases came from the rural area and 34 from the urban environment.

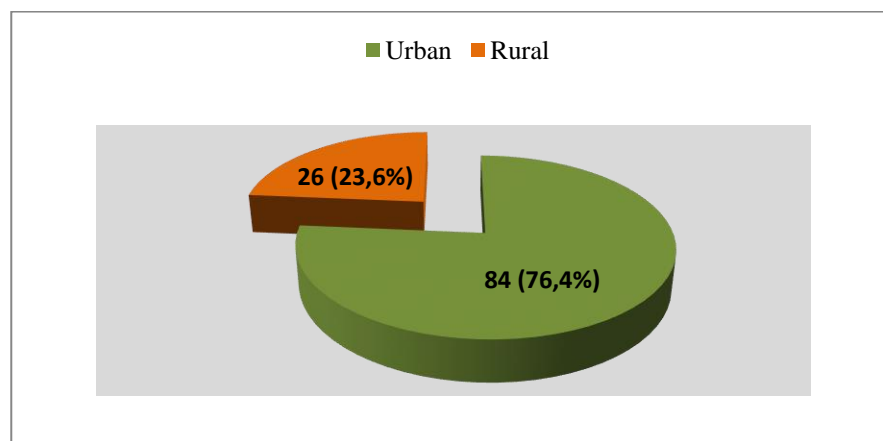


Figure 2. Distribution of cases by place of origin

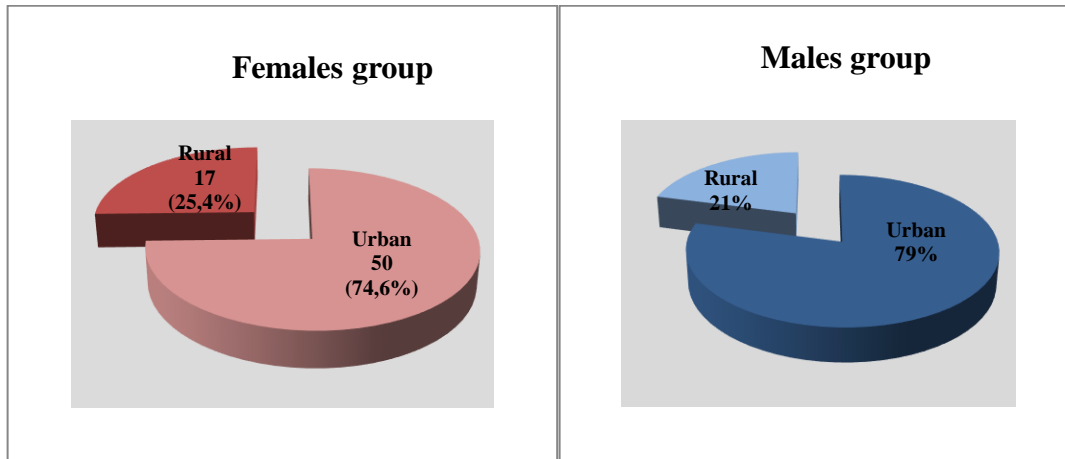


Figure 3. Distribution of cases by environment and gender

Analyzing the age of patients revealed a predominance of 40-49 year old patients in both the female and the male group.

We have established 4 age groups, namely: 30-39 years, 40-49 years, 50-59 years and 60-69 years.

In women, 7 cases were between 30-39 years of age, 34 were between 40-49 years of age, 19 were between 50-59 years of age, and 7 were aged between 60-69 years. In men, 4 cases were between the ages of 30-39 years, 21 were between 40-49 years of age, 12 were between 50-59 years of age and 6 cases were aged between 60-69 years. Thus, the analysis on the general study group comprised 11 cases aged 30-39 years, 55 cases aged 40-49 years, 31 cases aged 50-59 years and 13 cases aged 60-69 years.

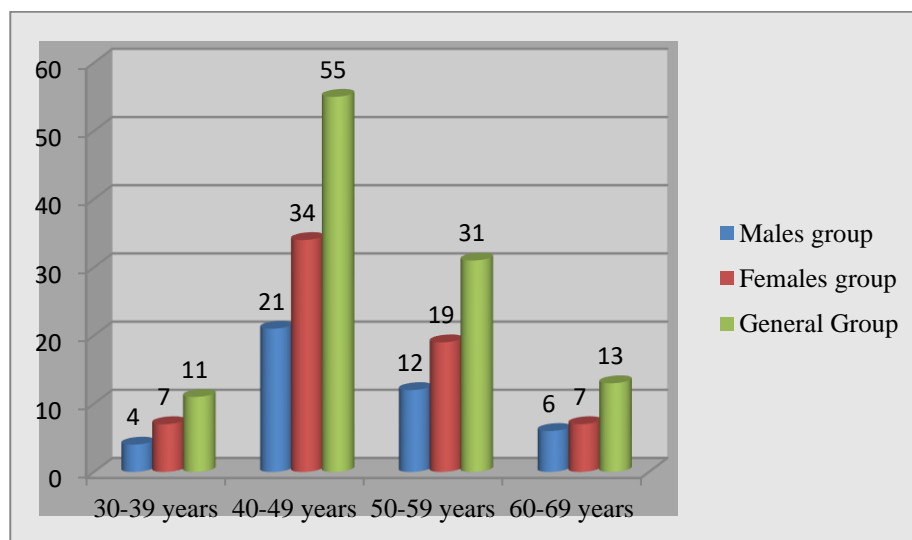


Figure 4. Distribution by age groups

Analyzing the height and weight data from the clinical observation sheets we calculated for each case included in the study the body mass index and we made a classification (according to WHO 2000) according to the assessed nutritional status.

The lower limit of BMI for obesity was 30 kg / m².

Cases with grade 1 obesity presented BMI values ranging from 30-34.9 kg / m², those with grade II obesity had BMI values between 35-39.9 kg / m² and those with Grade III obesity were characterized by BMI values above the 40 kg / m² limit.

Grade II obesity prevailed both in the female group (49 cases, respectively 73.1%) and in the male (25 cases and 58.1% respectively). The remaining cases in the female group were divided as follows: 12 cases with grade I obesity and 6 cases with grade III obesity. In the male group, 10 cases with grade I obesity and 8 cases with grade III obesity were identified.

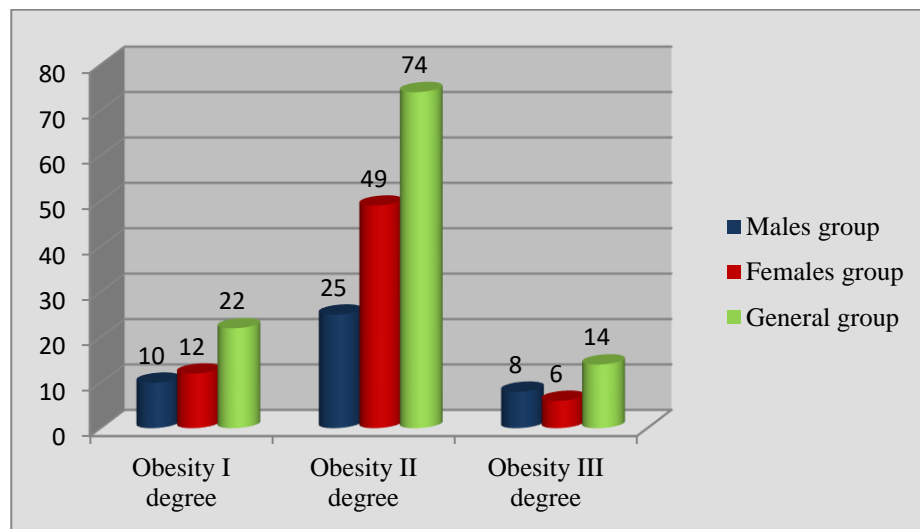


Figure 5. Distribution of cases by degree of obesity (male, female and general group)

Starting from the idea that not only quantity but also fat distribution is also a risk factor for cardio metabolic pathologies, the study looked at the analysis of the values of the abdominal circumference for each patient. According to the IDF (2009), abdominal circumference values ≥ 94 cm in men and ≥ 80 cm in women define Abdominal Obesity.

These values have been considered as reference in the current study. For both the female and the male group, 5 groups were formed in relation to the values of the AC, as follows:

- for women: 80-84.9 cm; 85-89.9 cm; 90-94.9 cm; 95-99.9 cm; and > 100 cm
- for men: 94-99.9 cm; 100-104.9 cm; 105-109.9 cm; 110-114.9 cm and > 115 cm.

In the female group, most cases (27 and 40.3% respectively) showed values of the AC in the range of 85-89.9 cm, and in the male group the most cases (12 and 27.9% respectively) showed values of AC in the range 100-104.9 cm.

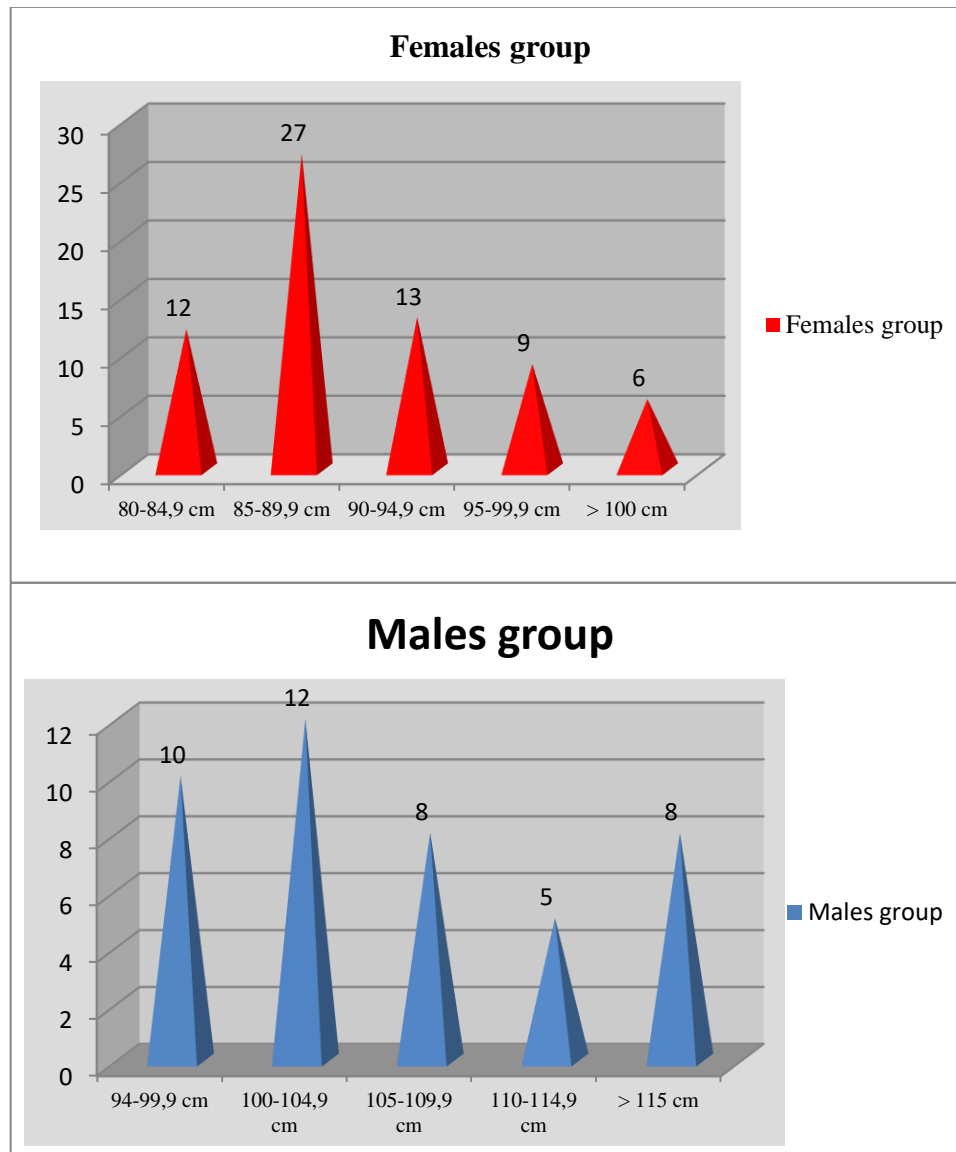


Figure 6. Abdominal circumference based on the patient's gender

In the female study group, the minimal value of the AC was 80 cm, the maximum value was 102 cm, the mean value was 89.92 cm, and the standard deviation calculated was 5.91.

In the male study group, the minimum AC was 95 cm, the maximum value was 116 cm, the mean value was 104.21 cm, and the standard deviation calculated was 6.7.

The serum total cholesterol, HDL cholesterol and triglycerides were analyzed for each case. Minimum, maximum, average, and standard deviation values were noted.

In terms of serum cholesterol values, in the female group, the mean value was 300.52 mg / dl, and in the male group it was 329.79 mg / dl.

**Table 1. Results on the analysis of the elements defining the lipid profile
Serum Total Cholesterol (mg/dl)**

	Women	Males
The minimum value	215	250
The maximum value	412	420
The average value	300,52	329,79
Standard Deviation	44,4	43,87

Analyzing the following parameter, namely serum HDL cholesterol values, mean values were 48.37 mg / dL for women and 46.44 mg / dL for males.

**Table 2. Results on the analysis of the elements defining the lipid profile
HDL Serum cholesterol (mg/dl)**

	Women	Male
The minimum value	40	37
The maximum value	60	58
The average value	48,37	46,44
Standard Deviation	5,96	9,02

Mean values for serum triglycerides were 196.62 mg / dl in the female group and 205.53 mg / dl in the male group.

**Table 3. Results on the analysis of the elements defining the lipid profile
Serum triglycerides (mg/dl)**

	Women	Male
The minimum value	130	145
The maximum value	287	310
The average value	196,62	205,53
Standard Deviation	40,5	47,6

Subsequently, based on these data, we analyzed the prevalence of cases with hypercholesterolemia (serum cholesterol > 200 mg/dl), hypertriglyceridemia (serum triglycerides > 150 mg/dl) with HDL cholesterol (HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women) and mixed dyslipidemia (association of altered lipid indices) within the general study group.

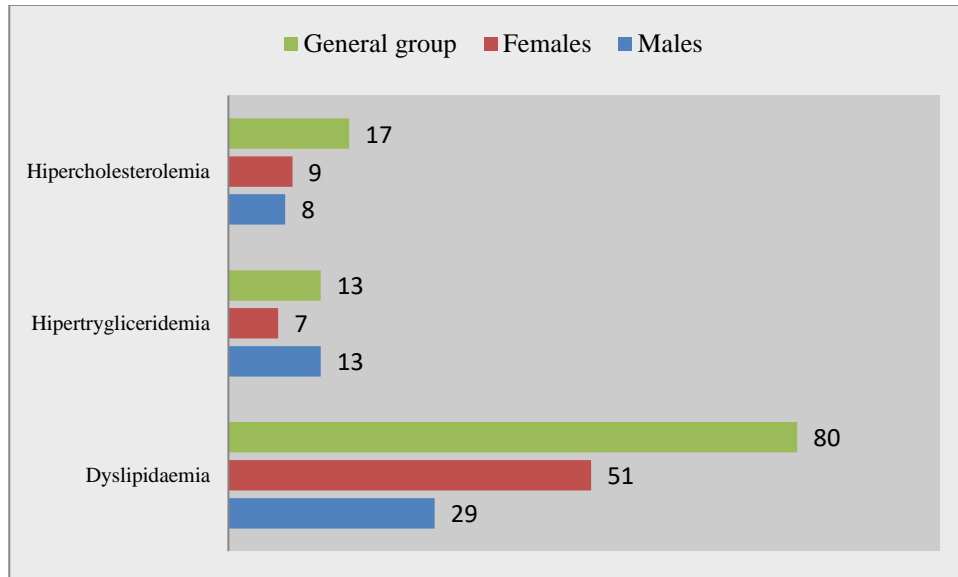


Figure 7. Changes in lipid metabolism in the female, male and general group

Therefore, the cases of mixed dyslipidemia prevailed in the female study group, where 51 cases (76.11%) and the male study group where 29 cases (67.44%) were identified. At the general batch level, the percentage for mixed dyslipidemia cases reached 72.7%.

Following the daily blood pressure values enrolled in the observation sheets of patients enrolled in the study and analyzing the medical history of hypertensive pathology, the results were as follows:

- In the female group, 55 obese patients associated increased blood pressure (above the 140/90 mmHg limit). Percentage, the recorded value was 82%.
- In the male group, 33 patients (76.7%) showed increased tensions.

It has also been taken into account that some patients have experienced normal tension, but under antihypertensive treatment. They were classified as hypertensives.

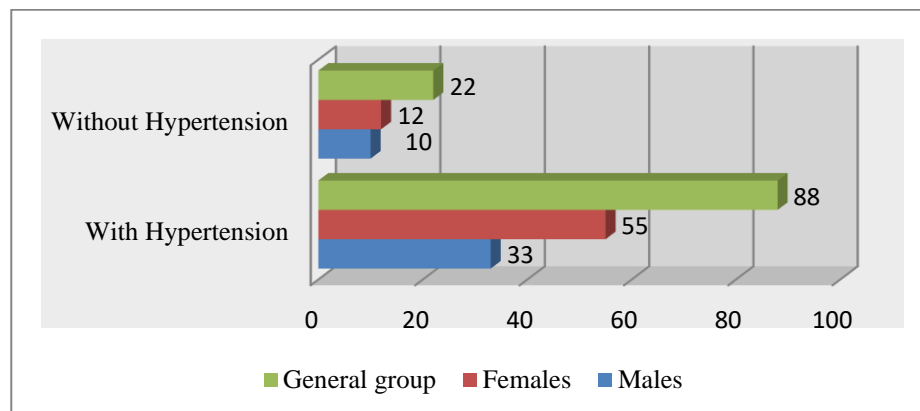


Figure 8. Analysis of the tension values in the female, male and general group

Hypertension prevalence in the overall study group was 80% (88 out of 110). 46 patients with obesity associated high blood sugar or were known with T2DM and were treated specifically (either with orally with or without insulin). Percentage was 68.6%. Within the male group, 25 cases associated T2DM and the prevalence was estimated at 58.1% of the cases. The analysis on the general study group showed that 64.5% of cases of obesity associated T2DM.

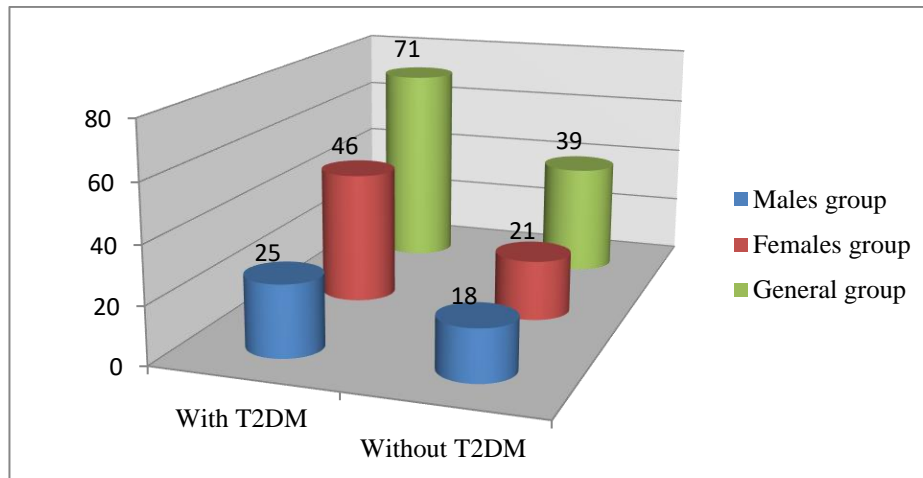


Figure 9. Analysis of blood glucose values in the female, male and general group

The results of the analysis of the study of risk behaviors for Obesity, HTA and DZ type II were obtained by analyzing the data recorded in the "behaviors" section of the clinical observation sheet. We have assessed for each case the presence or absence of behaviors considered at risk for the development of obesity, hypertension and diabetes.

The analysis focused on behaviors such as: unhealthy diet (hyper caloric, excess fat, carbohydrate and salt), smoking, sedentary

The results showed that 90% of all cases studied had one or more of the risk behaviors described above.

60 women (89.5%) and 39 men (90.6%) associated risk behaviors for developing overweight and cardio-metabolic pathologies.

55 women and 38 men with obesity have associated smoking. The overall percentage is relevant, 82% of women and 88.3% of boys associating this vice.

Unhealthy diet and sedentaryism were noted in most cases, both in the female and male bands, the overall value being 90.9% for the first parameter and 86.3% for the second.

Using data from liver ultrasound exploration, cases of obese patients were subdivided into the following categories: hepatic steatosis; with mild hepatic steatosis; with moderate hepatic steatosis; with severe hepatic steatosis.

Thus, we identified in the general study group: 6 cases of patients without steatosis-type liver disease, 20 obese patients with mild hepatic steatosis, 70 patients with moderate steatosis and 14 patients with severe steatosis.

The data correlated positively with degrees of obesity. Most cases experienced grade II obesity and moderate hepatic steatosis. The number of cases identified with grade III obesity was identical to the number of cases of severe hepatic steatosis.

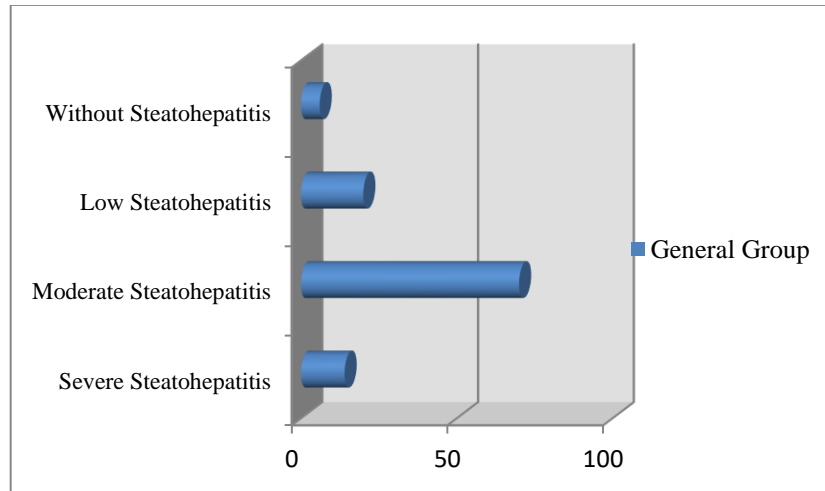


Figure 10. Analysis of steatose-type liver changes in obese patients

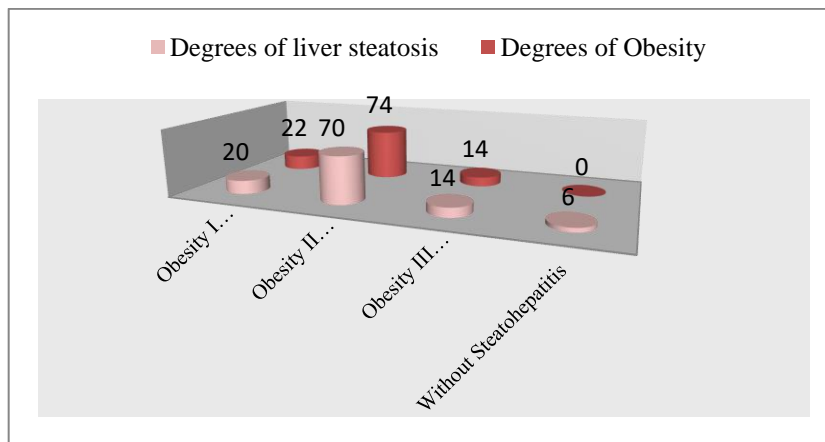


Figure 11. Correlations between obesity and the degree of hepatic impairment

Gallstones were identified in 32.7% of the cases of obese patients enrolled in the study.

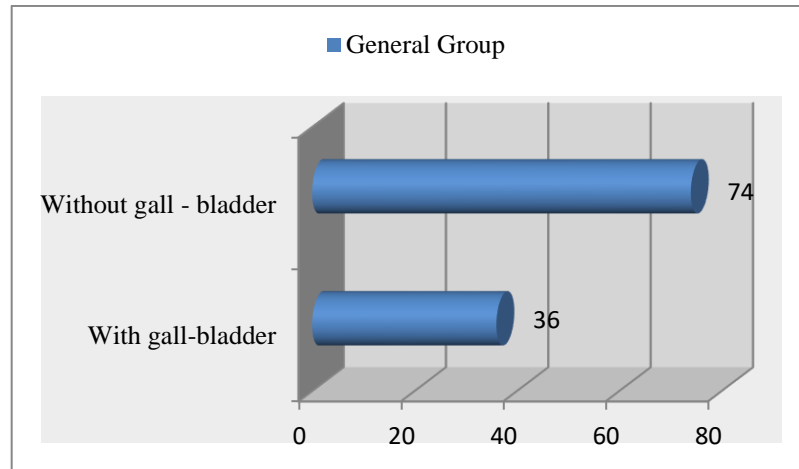


Figure 12. Results of association analysis Obesity - Gall bladder

DISCUSSIONS

Obesity is currently a pathology of epidemic proportions in most developed and developing countries.

The prevalence of obesity has grown steadily and alarmingly not only among the adult population but also in children and adolescents, a fact that is worrying for the medical world in terms of association with many cardiovascular, metabolic, osteoarticular, liver, kidney, neoplastic pathologies.

Obesity can have a significant impact on quality of life and may contribute to increased morbidity and overall mortality.

Defined as a chronic nutritional disorder, obesity is the increase in body weight due to fat, resulting from a lack of correlation between excess caloric intake and low energy expenditure. It actually translates into an excess of lipids in the body's composition by increasing the number of adipocytes but also their volume.

The main purpose of this work was to analyze the association of obesity with other chronic conditions such as: T2DM, hypertension, hypercholesterolemia, hypertriglyceridemia, dyslipidemia, liver steatosis, biliary lithiasis.

Analyzing the data from the literature, the prevalence of cases of obesity in relation to female/male sex is contradictory, depending largely on the studied region / country.

Numerous studies have shown a higher prevalence of obesity among the female population compared to the male population. However, in recent years, the trend is to equalize the percentages, the differences being not significant.

As it is known, obesity leads to numerous and important later complications, where dyslipidemia has an important place.

In the current study, serum total cholesterol, HDL cholesterol and triglycerides were analyzed for each obese patient, with the prevalence of hypercholesterolemia, hypotriglyceridemia and dyslipidemia being assessed.

Thus, cases of dyslipidemia prevailed both in the female study group (76.11%) and in the male study group (67.44%). At the general batch level, the percentage for dyslipidemia cases reached 72.7%.

Cases of hypercholesterolaemia/hypertriglyceridaemia were rarely identified in the current study group, 15.4% for hypercholesterolemia and 11.8% for hypertriglyceridemia. Dyslipidemia has numerous negative effects primarily by favoring atherogenesis⁵ and implicitly by increasing the risk of cardiovascular suffering.⁶

The degree and progression of atherosclerosis is closely related to the lipid profile and thus to the dyslipidemia condition.

Lipid abnormalities in obese patients include elevated serum triglycerides, VLDL cholesterol and apolipoprotein B as well as low HDL cholesterol. Low density lipoprotein particles are considered to be highly pro-atherogenic in view of the fact that they have low affinity for the LDL receptor and thus remain in circulation for a longer period of time. In addition, they can more easily penetrate into the arterial wall than the high density particles and form linkages with the intra-arterial proteoglycans.

Last but not least, these small particles are more susceptible to oxidation, which could lead to increased absorption by macrophages.⁷

Lipid profile abnormalities encountered in obese patients are the direct cause of insulin resistance and pro-inflammatory status induced by macrophages that invade adipose tissue. An essential abnormality is the overproduction of VLDL by the liver which contributes significantly to the increase in serum triglyceride levels⁸. The rate of VLDL secretion is largely dependent on the availability of triglycerides, in turn in relation to the level of fatty acids.

Analyzing the association between obesity and the presence of type II diabetes in the patients enrolled in the study, the percentage was 64.5% in the general group and the prevalence was higher in the female group, 68.6% versus 58, 1% in men.

Data from the literature show that the development risk of type II diabetes increases significantly with weight gain. Colditz et al., In a study published in 1995, assessed the risk of developing diabetes in excess of adipose tissue in 11,421 women. The results showed that for a weight gain of 5-9.9 kg the relative risk of developing diabetes is 1.9% and for a weight gain of 8-10.9 kg the relative risk is 2, 7%.⁹

In line with this observation, several studies have shown that weight loss is associated with a significant reduction in the risk of type II diabetes.

⁵ Adiels M, Olofsson SO, Taskinen MR, Boren J. *Overproduction of very low-density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome*. *Arterioscler Thromb Vasc Biol*. 2008;28:1225-1236.

⁶ Hoenig MR. *Implications of the obesity epidemic for lipid-lowering therapy: Non-HDL cholesterol should replace LDL cholesterol as the primary therapeutic target*. *Vascular Health and Risk Management* 2008;4(I) 143-156.

⁷ Kenneth R Feingold, Carl Grunfeld. *Obesity and dislipidemia*. NCBI, 2015.

⁸ Bays, H.E., et al., *Obesity, adiposity, and dyslipidemia: a consensus statement from the National Lipid Association*. *J Clin Lipidol*, 2013. 7(4): p. 304-83.

⁹ Colditz GA, Willett WC, Rotnitzky A et al. *Weight gain as a risk factor for clinical diabetes mellitus in women*. *Ann Intern Med*. 1995;122(7):481-486.

In a prospective 20-year study of 7,176 British men, the prevalence of diabetes cases was 11.4 per 1000 subjects among obese subjects and only 1.6 per 1,000 people in normal weight subjects.¹⁰

In the case of obese patients already known with type II diabetes, it has been shown that weight reduction is associated with better disease control.

This has been noted in the results of several studies, including the AHEAD (Action for Health in Diabetes) study, a randomized study of lifestyle intervention¹¹.

Starting from the idea that obesity can underlie the development of various cardiovascular pathologies, in the present study we have been looking at the prevalence of cases of hypertension in the 110 patients enrolled in the study.

In the general group we identified 88 cases (80% prevalence) with HTA, and the prevalence was differentiated by 82% in the female group and 76.7% in the male. Frequent association of obesity with high blood pressure and cardiovascular disease of atherosclerotic etiology has been reported more than 50 years ago. Recent advances in adipose tissue biochemistry have provided evidence of biochemical mechanisms involved in such associations.

Adipose tissue infused with monocytes has been shown to be an autocrine and endocrine organ, releasing pro-inflammatory cytokines, such as adiponectin and leptin. An increase in mRNA expression for 11 β hydroxysteroid dehydrogenase and for hexose-6 phosphate dehydrogenase was detected in the adipose tissue of obese women, resulting in an acceleration of the synthesis of cortisol and aldosterone.

Adipose tissue also contains components of the renin-angiotensin-aldosterone system, with an increase in angiotensin II generation in obese adipose tissue, leading not only to increased blood pressure, but also to the development of oxidative stress and inflammation¹², and the decrease consecutive adiponectin production would contribute to resistance to insulin. Excessive free fatty acids in the circulation inhibit nitric oxide synthase and implicitly the production of relaxation factor derived from endothelium, a mechanism that could contribute to the occurrence of high blood pressure.¹³

Several studies have shown positive association between obesity and development of hypertension, cardiac arrhythmias (especially atrial fibrillation)¹⁴, angina pectoris, congestive heart failure, myocardial infarction, stroke¹⁵

¹⁰ Wannamethee SG, Shaper AG, Walker M. *Overweight and obesity and weight change in middle aged men: impact on cardiovascular disease and diabetes*. J Epidemiol Community Health. 2005;59(2):134–139.

¹¹ Look AHEAD Research Group. Pi-Sunyer X, Blackburn G, Brancati FL, et al. *Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial*. Diabetes Care. 2007;30(6):1374–1383.

¹² Steinberg H.D., Tarshoby M., Menestel R. et al. *Elevated circulating free fatty acid levels impair endothelium – dependent vasodilatation*. J Clin Invest, 1997, 100, 1230-1239.

¹³ Davda R.K., Stepniakowski K.T., Ullian M.E. et al. *Oleic acid inhibits endothelial nitric oxide synthase by a protein kinase C independent mechanism*. Hypertension, 1995, 26, 764-770.

¹⁴ Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. *The disease burden associated with overweight and obesity*. JAMA. 1999;282(16):1523–1529.

¹⁵ Klein S, Burke LE, Bray GA, et al. *American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for*

One of the most representative studies of the association between obesity and cardiovascular risk was the Framingham study, conducted on 5209 subjects¹⁶.

The data provided by the follow-up of subjects for 30 years demonstrated the clear difference between the risk of cardiovascular disease development in obese patients (78.8%) compared to the same risk in non-weighted patients (54.8%).¹⁷

The SEPHAR study, the study of the prevalence of hypertension and the risk assessment of cardiovascular risk in Romania, was conducted in 2005 and tracked a lot of 2017 subjects over the age of 18 years. The data provided by this studio showed that the prevalence of primary hypertension in obese subjects is very high - 54.1% (52% in the female group and 58% in the male group), significantly higher than the prevalence of the same pathology in normoponderal¹⁸.

Analyzing the prevalence of digestive complications associated with obesity, the current study analyzed the liver and cholecystic echographic structure and made assessments of the degree of liver steatosis and the presence / absence of biliary lithiasis.

Thus, in the general group we identified moderate hepatic steatosis at 63.6%, and biliary lithiasis in 32.7% of the cases studied. Moreover, degrees of hepatic steatosis (mild, moderate and severe) correlated positively with the degree of obesity identified in patients.

Out of 22 patients with grade I obesity, 20 experienced mild hepatic steatosis; of 74 patients with grade II obesity, 70 had moderate hepatic steatosis, and 14 patients with grade III obesity had severe hepatic steatosis.

Data from the literature signals differences in the visceral adipose tissue function compared to subcutaneous adipose tissue.

Subcutaneous adipose tissue is the major source of leptin and adiponectin, and is also more susceptible to insulin action. Visceral adipose tissue is more susceptible to adrenergic stimuli that lead to increased lipolysis and the release of non-esterified fatty acids that reach the liver through the portal vein.

Most proinflammatory cytokines such as tumor necrosis factor alpha, interleukin 6 as well as angiotensinogen and plasminogen activator inhibitor mostly originate from visceral adipose tissue¹⁹.

Excess free fatty acids and proinflammatory cytokines in the portal circulation in association with hyperinsulinism lead to lipid loading of the liver and stimulation of liver synthesis of lipoproteins and proteins.

Regarding the association of obesity-lymphocyte biliary, as previously stated, in the current study, 32.7% of obese patients presented biliary calculus images on ultrasound examination.

Data from literature shows that obesity is a risk factor for this digestive pathology²⁰. Cholesterol production accounts for over 80% of all cases of biliary lithiasis. Obesity is an important risk factor in cholesterol formation by cholesterol overloading of the bile and decrease

professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation*. 2004;110(18):2952–2967.

¹⁶ Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. *Overweight and obesity as determinants of cardiovascular risk: the Framingham experience*. *Arch Intern Med*. 2002;162(16):1867–1872.

¹⁷ Fox CS, Pencina MJ, Wilson PW et al. *Lifetime risk of cardiovascular disease among individuals with and without diabetes stratified by obesity status in the Framingham heart study*. *Diabetes Care*. 2008;31(8):1582–1584.

¹⁸ Dorobanțu Maria, Bădilă Elisabeta, Darabont Roxana et al. *Studiul SEPHAR-studiu de prevalență a hipertensiunii arteriale și evaluare a riscului cardiovascular în România*. *Revista Română de Cardiologie*, vol.XXI, Nr.3, 2006.

¹⁹ Wajchenberg BL, Gianella-Netto D, Da Silva MER et al. *Depot - specific hormonal characteristics of subcutaneous and visceral adipose tissue and their relation to metabolic syndrome*. *Horm Metab Res* 2002; 34:612-621

²⁰ Shaffer EA. *Gallstone disease: epidemiology of gallbladder stone disease*. *Best Pract Res Clin Gastroenterol* 2006;20:981-96.

in bile vesicle motility. There is a linear correlation between the body mass index (BMI) and the risk of biliary lithiation, so a woman with a BMI of 45 kg / m² has a 7-fold higher risk of developing biliary calculi than a woman with BMI less than 24 kg / m².²¹ Numerous studies support the important role of abdominal obesity in lithogenesis through the increased insulin resistance of abdominal fat. Tsai et al. Established a significant correlation between abdominal obesity index (abdominal circumference, waist-to-hip ratio) and increased cholecystectomy in women (waist / hip ratio = 0.86, RR = 1.39, 1.66, p < 0.0001), independent of IMC (42). Calcification of the waist > 102.6 cm in males determined a relative risk of 2.29 (95% CI 1.69-3.11, p < 0.0001) of symptomatic biliary lithiasis versus those with a circumference < 86.4 cm.²²

CONCLUSIONS

- ♣ Obesity is an important public health problem, with increasing prevalence and multiple complications, especially with increased frequency of dyslipidemia, type 2 diabetes and hypertension.
- ♣ In Romania, the prevalence of metabolic syndrome is estimated at 44%, 43% among men and 45% among women.
- ♣ Metabolic syndrome is associated with increased risk of a variety of pathologies including diabetes mellitus, peripheral arterial disease, non-alcoholic liver steatosis, polycystic ovary syndrome, biliary lithiasis, asthma, articular degenerative disease, depression, sleep apnea syndrome and some forms of cancer (prostate, breast, endometrium, colorectal).
- ♣ The current concept of adipose tissue is that it is an organ that mediates specific functions such as conserving energy reserves, hormone secretion and an immune role. In obesity there is an increase in fat mass, especially by increasing the size of fat cells, although their number can be increased especially in obese childhood onset individuals.
- ♣ Obesity determines insulin resistance is a pathological condition characterized by a suboptimal response of peripheral tissues to the action of insulin.
- ♣ Generally viewed, the metabolic syndrome is a cumulative risk factor that includes central obesity, hyperglycemia, atherogenic dyslipidemia and elevated blood pressure.
- ♣ The study was retrospective, with the case studies of 110 obese patients, and the data used were taken from the clinical observation sheets.
- ♣ Female lot represented 61% and male 39%, half of patients aged 40-49 years and 76.4% with urban residence.
- ♣ Mixed dyslipidemia prevailed both in the female study group (76.11%) and in the male study group (67.44%). At the general batch level, the percentage for mixed mixed dyslipidemia cases reached 72.7%.
- ♣ 64.5% of patients enrolled in the study had T2DM, the prevalence being higher in the female group, 68.6% compared to 58.1% in males.

²¹ Stampfer MJ, Maclure KM, Colditz GA, et al. *Risk of symptomatic gallstones in women with severe obesity.* Am J Clin Nutr 1992; 55: 652-658.

²² Tsai C-J, Leitzmann MF, Willett WC et al. *Central Adiposity, regional fat distribution, and the risk of cholecystectomy in women.* Gut 2006; 55: 708-714.

- ♣ In the general group we identified 88 cases (80% prevalence) with HTA, and the prevalence was 82% in the female group and 76.7% in the male.
- ♣ We identified moderate hepatic steatosis in 63.6% of the cases studied.
- ♣ The degrees of hepatic steatosis (mild, moderate and severe) correlated positively with the degree of obesity identified in patients.
- ♣ Obesity is an important risk factor in the formation of cholesterol calculi by cholesterol overloading of the bile and the decrease in bile duct motility. In the current study we identified biliary lithiasis in 32.7% of the analyzed cases.

COMPLIANCE WITH ETHICS REQUIREMENTS. The authors declare no conflict of interest regarding this article.

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THE ALTERATION OF LIPID METABOLISM IN PREDIABETES

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ABSTRACT:

DYSLIPIDEMIA IS ONE OF THE KEY FACTORS OF INITIATION, PROGRESSION AND COMPLICATION OF THE ATHEROSCLEROSIS PROCESS, BEING AN INDEPENDENT RISK FACTOR ASSOCIATED WITH INCREASED CARDIOVASCULAR MORBIDITY AND MORTALITY

BEFORE REACHING DIABETES, IT WAS FOUND THAT A MAJORITY OF PATIENTS HAD A PREDIABETIC PHASE. STATISTICS SHOW THAT ABOUT 30% OF ROMANIANS ARE IN THE PREDIABETIC PHASE, WITH OR WITHOUT RISK, THAT IN THE COMING YEARS THEY WILL EVOLVE TO DIABETES ITSELF.

THE PURPOSE OF THE STUDY WAS TO DETERMINE THE PREVALENCE OF PREDIABETES, DYSLIPIDEMIA AND TO ESTABLISH CORRELATIONS BETWEEN THE PRESENCE OF DYSLIPIDEMIC RISK FACTORS AND THE PRESENCE OF PREDIABETES.

THE STUDY GROUP CONSISTED OF 289 PATIENTS, WITH 141 MEN AND 148 WOMEN PARTICIPATING IN THIS DESCRIPTIVE OBSERVATIONAL STUDY.

ALTERATIONS IN LIPID METABOLISM ARE COMMON IN PREDIABETIC PATIENTS. DYSLIPIDEMIA WAS FOUND IN APPROXIMATELY EQUAL PROPORTIONS IN BOTH WOMEN AND MEN.

DYSLIPIDEMIA AND PREDIABETES ARE OFTEN PRESENT AT THE SAME TIME IN A PERSON.

KEY WORDS: DYSLIPIDEMIA, PREDIABETES, DIABETES MELLITUS

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INTRODUCTION

Dyslipidemia is one of the key factors of initiation, progression and complication of the atherosclerosis process, being an independent risk factor associated with increased cardiovascular morbidity and mortality⁵. Before reaching diabetes, it was found that a majority of patients had a prediabetic phase.

Statistics show that about 30% of Romanians are in the prediabetic phase, with or without risk, that in the coming years they will evolve to diabetes itself. In children, the early presence of prediabetes may increase the risk of developing diabetes mellitus (DM) in adolescence. However, it is accepted that, in children and adolescents, prediabetes can readily return to normal blood sugar.

Statistics show that adolescents aged 12-15 years have a significantly higher prediabetes compared to other ages; in boys, prediabetes is 2.4 times more frequent than in girls. In adults, prediabetes can be aggravating health consequences and associated with retinopathy, neuropathy, high blood pressure, high total cholesterol (TC) and triglycerides (TG), polycystic ovarian syndrome and some cardiovascular diseases⁶.

The purpose of the study was to determine the prevalence of prediabetes, dyslipidemia and to establish correlations between the presence of dyslipidemic risk factors and the presence of prediabetes.

MATERIAL AND METHODS

The population examined between 2016 and 2017 was from urban area in Dolj county. Our study group was composed by 289 patients. In this descriptive observational study responded 141 men and 148 women.

The mobilization was randomized from the patients who presented themselves to the outpatient clinic without taking into account the family doctor on whose list the patient was enrolled.

We analyzed the following data: demographic data (age, sex, background), anthropometric data (weight, height, body mass index), physiological personal history, pathological personal history and heredocolateral history of diabetes, hypertension, dyslipidemia, myocardial infarction, obesity, autoimmune diseases, etc.).

Venous blood was collected from which the following tests were performed: serum creatinine, total cholesterol, HDL-cholesterol, LDL-cholesterol calculated with Friedwald formula, triglycerides, uric acid, serum hemoglobin.

Preliminary dates on measured clinical parameters were entered into the computer in the database tables in the Microsoft Excel module in the Microsoft Office 2010 Professional and Office 365.

⁵ International Diabetes Federation – IDF Diabetes Atlas; 6th edn. Brussels, Belgium: International Diabetes Federation, 2013. <http://www.idf.org/diabetesatlas>

⁶ American Diabetes Association (ADA); *Clinical practice recommendations – Diagnosis and classification of diabetes mellitus*, Diabetes Care. 2014; 37 (Suppl 1), S81-S90

RESULTS

The study group consisted of 289 patients, with 141 men and 148 women participating in this descriptive observational study.

The first clinically evaluated parameter was the distribution of patients studied by gender. As can be seen from the data centralized in Table 1, the Male/Female ratio was approximately 1:1.

Table 1: Distribution of cases by gender

Gender	No. of cases	%	Male/Female Ratio
Male	141	48,78	0,95
Female	148	51,21	
TOTAL	288	100	

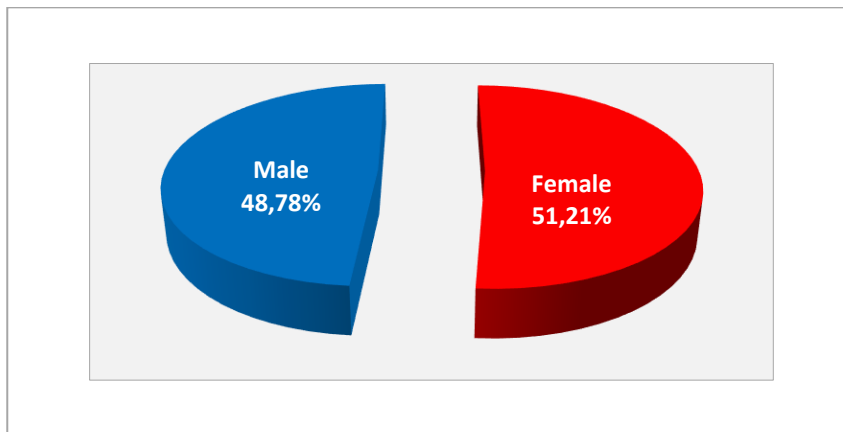


Figure 1. Distribution by gender of the studied lot

The patients included in the study group were generally adults and especially the elderly. The dispersion age range was between 40 -87 years (Table 2).

Table 2. Statistical Age Parameters

Statistical parameter	Value
<i>The youngest age</i>	40 years
<i>The oldest age</i>	87 years
<i>Average age</i>	65 years
<i>Std. Dev.</i>	10 (55 – 75 years)
<i>Std. Dev. = Standard deviation</i>	

The age group that included the majority of patients (95 patients, almost 33% of cases was between 60 - 69 years).

Using the stratification of patients by age, we found that more than half of them (80%) were over 60 years, making the average age of the patients 65 years and the agglomeration interval in most cases, between 60 - 75 years (Figure 2).

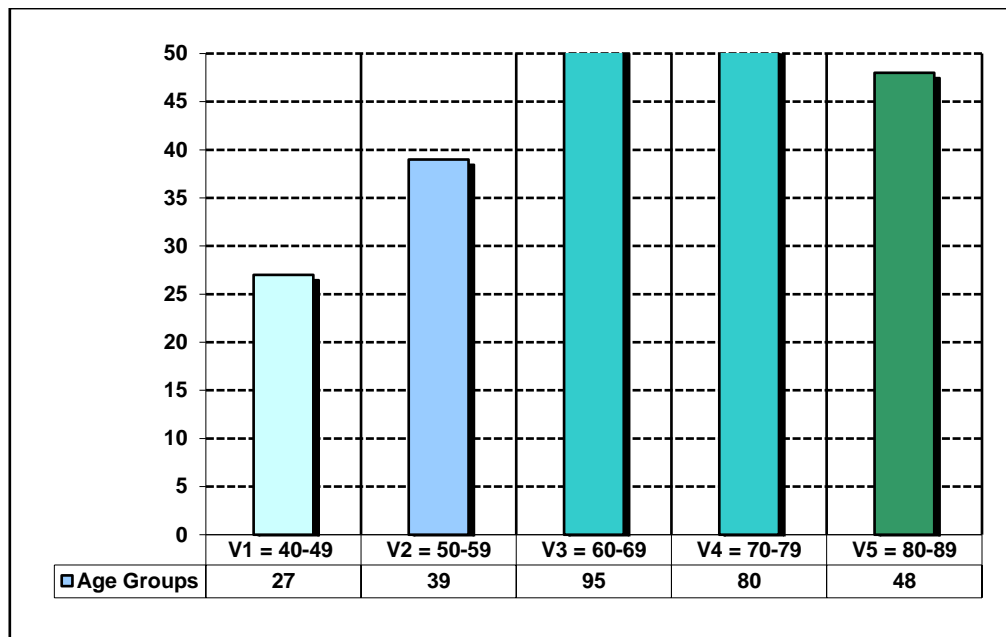


Figure 2. Distribution of patients by age group

The prevalence of dyslipidaemia was 55.70% (Figure 3), insignificantly higher in women than in men 54.72% vs 56.73%) ($p = 0.228$). According to the results of the PREDATORR study, in Romania, the prevalence of dyslipidemia is much higher, 81%.

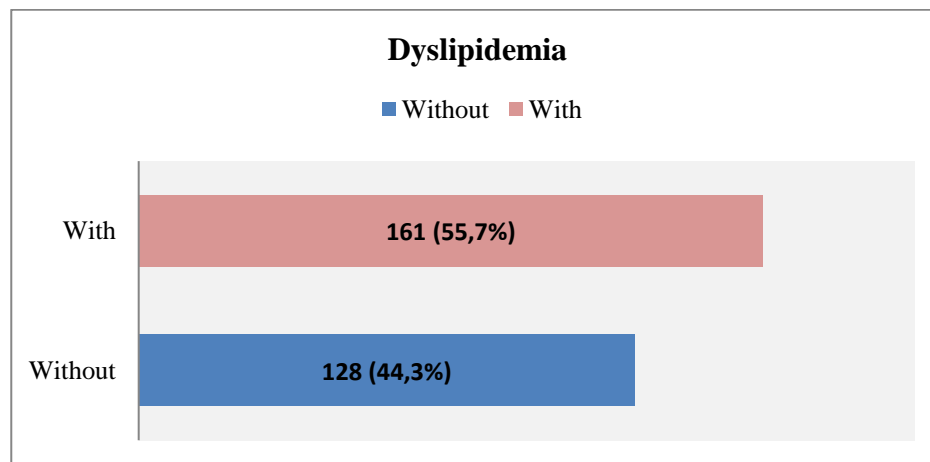


Figure 3. Prevalence of dyslipidemia in the studied group

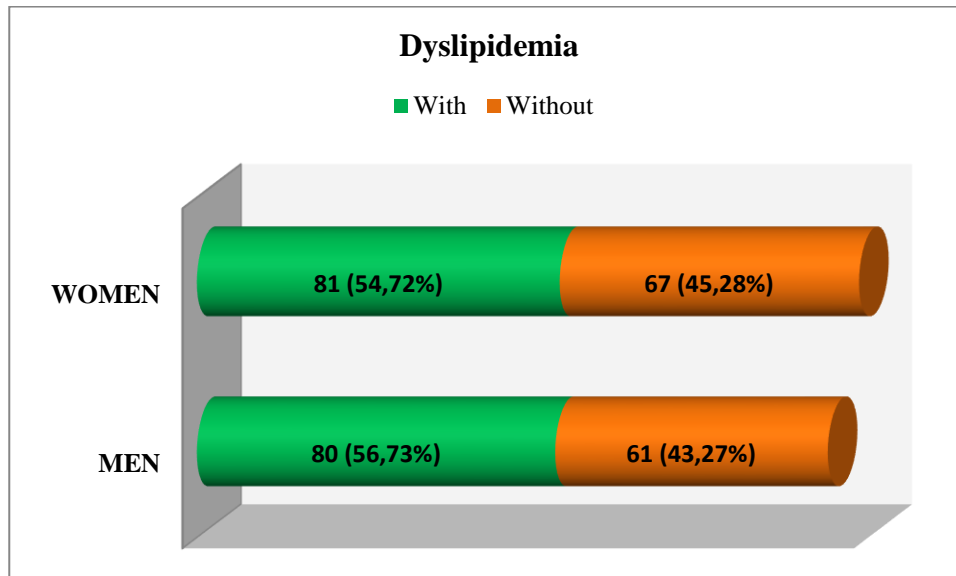


Figure 4. Prevalence of dyslipidemia by gender

In Romania, dyslipidemia is around 30%, and in 2008 according to the study SEPHAR (Study for the Prevalence of Hypertension and Cardiovascular Risk in Romania)⁷ there was a prevalence of hypercholesterolemia of 40% in the adult population.

In 2013, according to the PREDATOR study, the prevalence of dyslipidemia involving two or more fatty parameters with pathological values was 60.7%.

Prediabetes had a prevalence of 11.76%, significantly higher among women (19.59% vs 14.7%) ($p = 0.002$).

⁷ Cintează M, Pana B, Cochino E, et al; *Prevalence and control of cardiovascular risk factors in Romania: Cardiozone national study. Mædica – A Journal of Clinical Medicine*, 2007, 2(4): 277-288

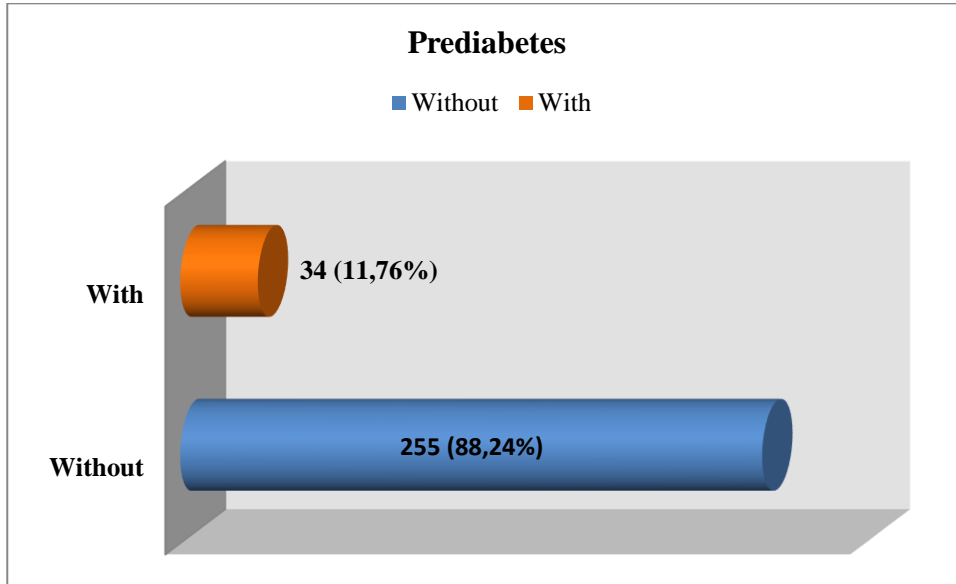


Figure 5. Prevalence of prediabetes in the studied group

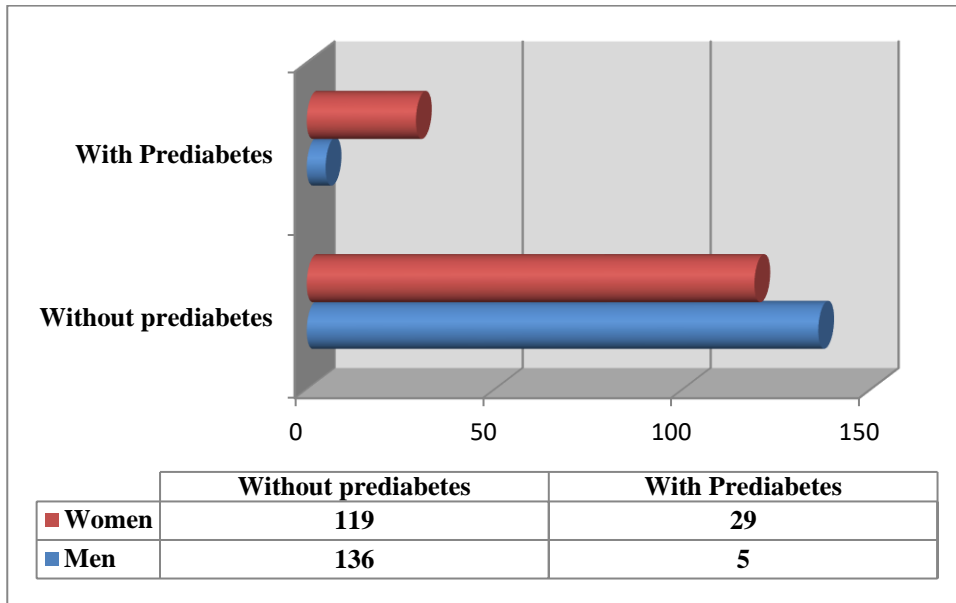


Figure 6. Prevalence of prediabetes by gender

Diabetes was recorded in 3.8% of subjects, significantly higher in males (4.96% vs. 2.70%) (p = 0.047).

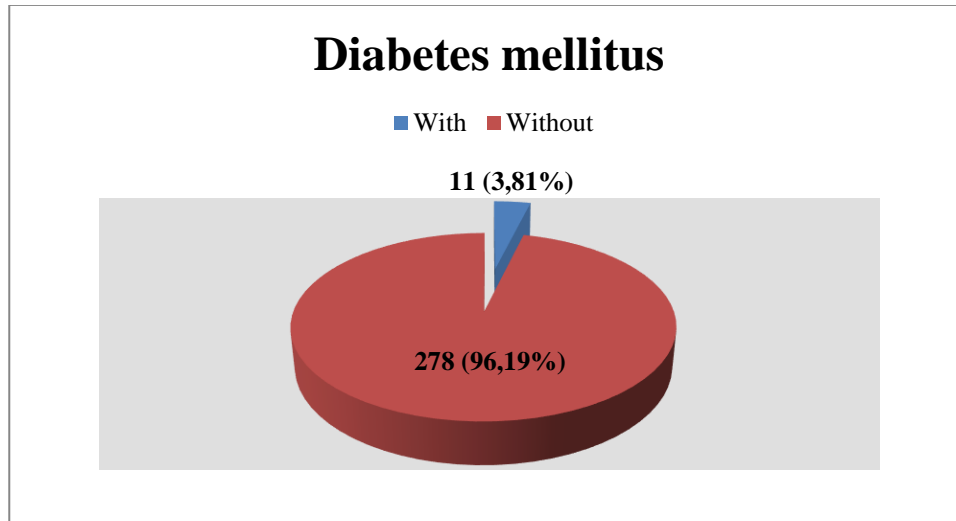


Figure 7. Prevalence of diabetes in the studied group

In 2011, the National Diabetes Register shows a national prevalence of 5.3%, 10.2% for males and 7.4% for women, according to the PREDATORR study.

By comparing the data from the PREDATORR study⁹, completed in 2014, and the results obtained in our study, we have the following results: national prediabetes is found to be 18.4%, in our study 11.76%.

As for diabetes, the national level is 11.67% and in our study it is 3.8%. By detailing gender, prediabetes in women is 19.5% in the PREDATORR study, 19.59% in our study, and 16.9% in males at national level, in our study 14.7%; diabetes is found in the PREDATORR study of female at 7.4%, in our study is 2.7% and in male is 10.2% versus 4.96% in our study.

CONCLUSIONS

Alterations in lipid metabolism are common in prediabetic patients. Dyslipidemia was found in approximately equal proportions in both women and men. Dyslipidemia and prediabetes are often present at the same time in a person.

COMPLIANCE WITH ETHICS REQUIREMENTS. The authors declare no conflict of interest regarding this article.

ACKNOWLEDGEMENT. All the authors contributed equally to this study and they all have the same rights.

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ASPECTS OF METABOLIC SYNDROME

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ABSTRACT

METABOLIC SYNDROME IS THE NAME FOR A GROUP OF DISORDERS THAT RAISE A PATIENT'S RISK FOR HEART DISEASE AND OTHER HEALTH PROBLEMS. MOST OF THE DISORDERS ASSOCIATED WITH METABOLIC SYNDROME HAVE NO SYMPTOMS (ALTHOUGH A LARGE WAIST CIRCUMFERENCE IS A VISIBLE SIGN) AND THUS IT CAN BE CONSIDERED A SILENT TRIGGER.

METABOLIC SYNDROME HAS BECOME A MORE COMMON HEALTH PROBLEM DUE TO A RISE IN OBESITY RATES AMONG ADULTS NOWADAYS.

FOR EFFECTIVE PREVENTION AND TREATMENT APPLIED AS EARLY AS POSSIBLE, IT IS VERY IMPORTANT TO IDENTIFY RISK FACTORS AND TO RAISE PATIENT AWARENESS FOR THIS CONDITION, ESPECIALLY BECAUSE A NUMBER OF MEASURES THAT ARE REQUIRED FOR THEM SUCH AS QUITTING SMOKING, ADOPTING A HEALTHY LIFESTYLE WITH A HEALTHY DIET AND INCREASING DAILY ACTIVITY, ARE AVAILABLE TO ANYONE.

KEY WORDS: METABOLIC SYNDROME, RISK FACTORS, SEDENTARISM, SMOKING

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INTRODUCTION

Consumption of food with a high degree of processing and / or high caloric density (foods with high carbohydrate and saturated fat content), the combination of this specific diet with the consumption of alcohol and tobacco as well as with an unhealthy rhythm of life (characterized by lack of physical activity, a marked decrease in rest time, a chaotic meal program, etc.), all of these unfortunately lead to a considerable increase in the risk of developing metabolic syndrome.⁸

The profound metabolic disorders associated with this syndrome is defined as a combination of symptoms that are often cumulative (abdominal obesity, dyslipidemia, low glucose tolerance, arterial hypertension) and may lead to the development of major-impact conditions on health status - cardiovascular diseases and type 2 diabetes.⁹

IDF (International Diabetes Federation) quantifies the parameters and diagnostic criteria for the metabolic syndrome as follows: For a person to be diagnosed with this condition, the mandatory presence of abdominal obesity (measured by abdominal circumference over 94 centimeters in men and 80 centimeters in women) associated with at least two of the following pathological conditions: high blood pressure (over 130/85 mm Hg) or treated HTA, dyslipidemia (triglyceride concentration greater than 150 mg% or, as with HTA, treated dyslipidemia), low serum HDL (lower than 40 mg% in men, respectively less than 50 mg % in women) and elevated blood glucose (more than 100 mg% or the presence of type 2 diabetes in treatment), all correlated with the values of the Body Mass Index (BMI)¹⁰.

In the definition of metabolic syndrome, other parameters (abnormal distribution of body fat, changes in vascular endothelium, pro-inflammatory and prothrombotic status, etc.) can also be associated (according to IDF).

MAIN TEXT

I. THE AIM OF THE STUDY

The purpose of this study was to identify this condition, in accordance with the IDF 2015 parameters of the Metabolic Syndrome, in a number of 156 patients admitted to the Medical Clinic of Railway Clinical Hospital of Craiova; the study was conducted over two years (January 2016-November 2017).

II. MATERIAL AND METHOD

The inclusion of patients in this study was performed by establishing age-based samples (three age groups, respectively 20-40 years, 40-60 years and over 60 years), while pursuing the demographic variables (age, gender, the residence environment) as well as the evaluation of metabolic syndrome by monitoring, during hospital admission, the parameters defined by the International Diabetes Federation in 2015 for establishing this diagnosis.

In order to better study the link between metabolic syndrome and an unhealthy lifestyle, we have taken into consideration (although not defining by IDF in establishing this diagnosis)

⁸ Yoo JS, Jeong JI, Park CG, et al. : [Impact of life style characteristics on prevalence risk of metabolic syndrome]. J Korean Acad Nurs, 2009, 39: 594-601.

⁹ Wilson PZF, Kannel WB, Silbershatz H, D'Agostino RB. Clustering of metabolic factors and coronary heart disease. *Arch Intern Med.* 1999; 159:1104-1109

¹⁰ International Diabetes Federation – IDF Diabetes Atlas; 6th edn. Brussels, Belgium: International Diabetes Federation, 2013. <http://www.idf.org/diabetesatlas>

other anamnestic data from the patients observation sheets included in the study: alcohol and tobacco products, disordered meals as well as information on eating habits (high fat consumption).

Since the Railway Clinical Hospital of Craiova is mostly a hospital for chronic patients, it was found that in the two years of study there were 9 persons who had multiple admissions during the research period.

III. RESULTS

For the first year of study (2016), 84 patients were included in the study for which the observational sheet data allowed the metabolic syndrome assessment. Gender ration (M/F) for the first year of study was 1.54 – with 51 men (60.71%) and 33 women (39.29%). In the second year of study (2017), 72 patients were included, thus, the gender ratio (M/F) was 1,1- with 38 men (52.77%) and 34 women (47.23%) (*Figure 1*)

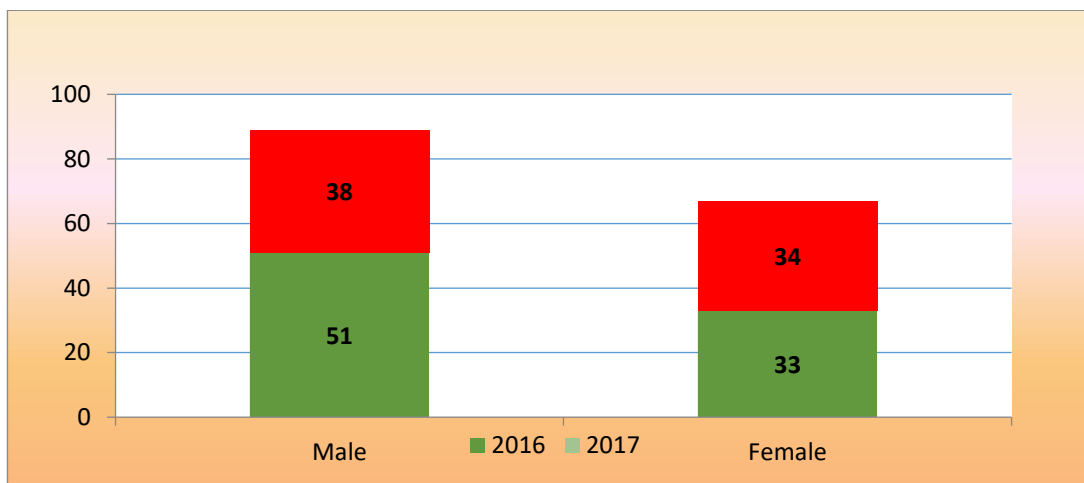


Figure 1. Gender distribution of patients in the study

Because during the study, there were 9 patients (6 women and 3 males) who were admitted in the both years, the studied groups had an overlapping area of 5.77%; these 9 patients were followed during the study and changes in food and lifestyle behavior, in close connection with the potential changes in their metabolic status.

The distribution by resident population of the two studied lots is similar, in correlation with the specificity of the medical unit in which the study was conducted. Thus, we can observe, that in the both studied years, a large proportion of patients came from urban area, in contrast with the patients who came rural areas (*Figure 2*). This fact can be explained by a greater accessibility of patients living in urban areas to medical services.

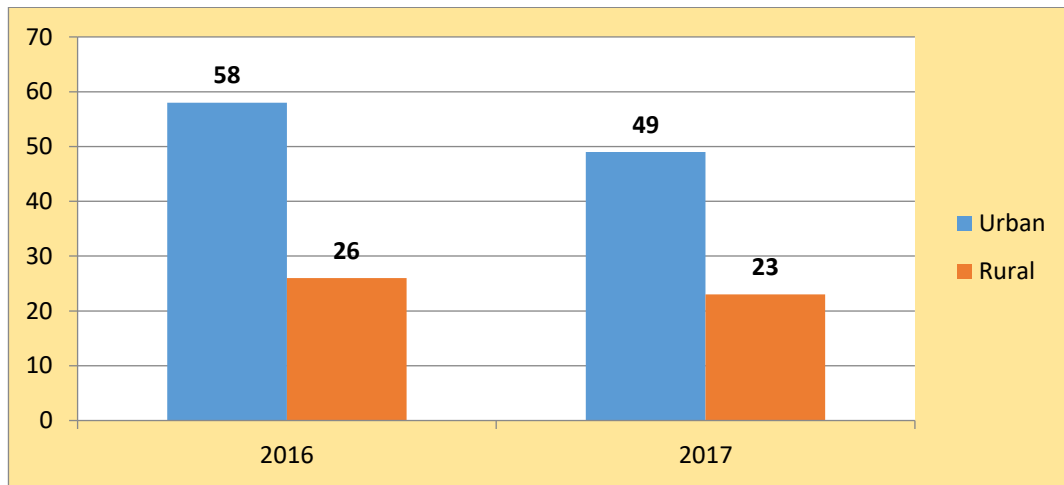


Figure 2. Residence area distribution of patients in the study

Regarding patients distribution according to age groups, we observed that in the both studied years, there was an increased number of patients in the 40-60 year old group. Thus, for 2016 distribution by age group was 32 patients (38.09%) in the 20- 40 years old group, 38 patients (45.23%) between 40-60 years and 14 patients (16.68%) over 60 years old. In 2017 proportions are relatively similar – 21 patients (29.16%) aged between 20 and 40 years, 34 patients (47.22%) between 20-60 years old and 17 patients (23.62%) aged over 60 years (*Figure 3*).

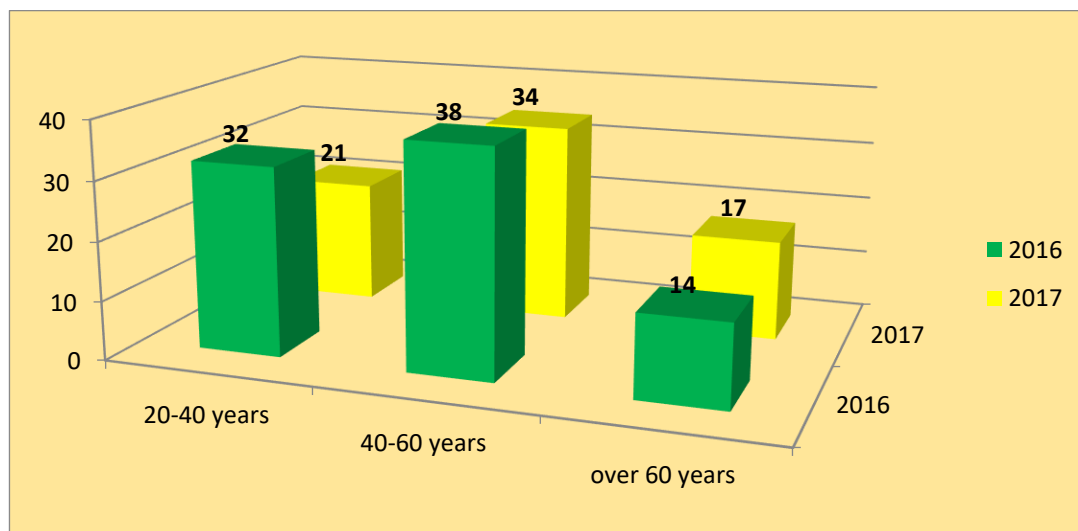


Figure 3. Number of patients by age groups

With regard to the distribution by sex and age groups of the patients under study, we observed a higher prevalence of female patients in both years for 20-40 years old group (18 patients in 2016 and 15 patients in 2017) compared to 14 male patients in 2016 and 6 male patients in 2017

on the same age range) but also the predominance of male patients for the other two age ranges studied. Thus, for the age range of 40-60 years, the sex distribution of patients was the following: 29 male patients for the 2016 and 14 male patients for the 2017 lot; in the case of patients older than 60 years, 8 male patients were included in the study in 2016 and 12 in 2017 (*Figure 4*).

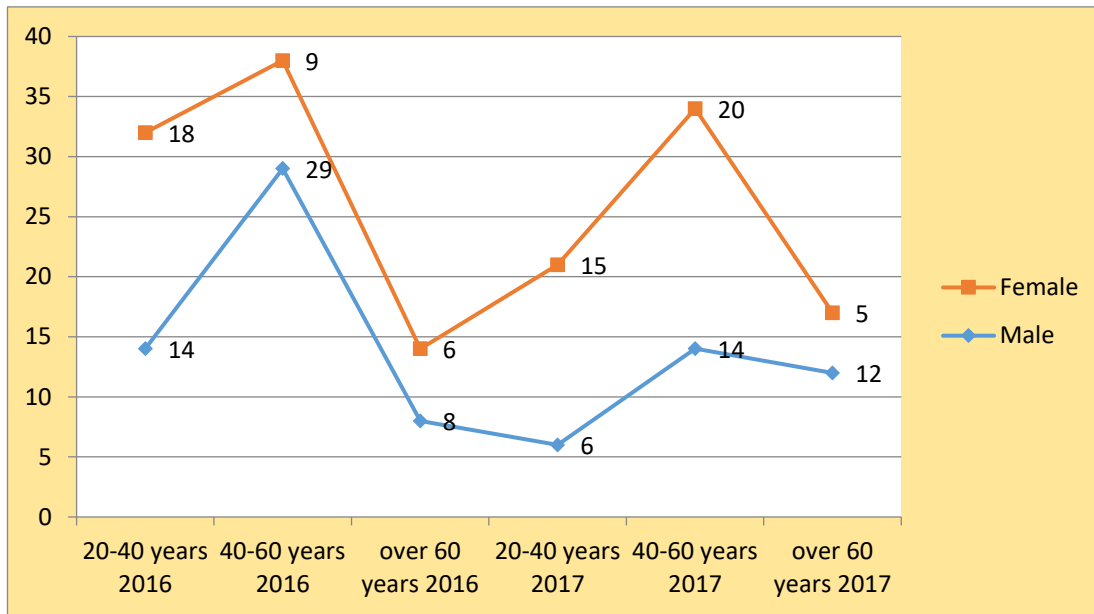


Figure 4. Distribution of patients by age groups and sex

From the detailed observational sheet analysis of these patients, following the diagnostic parameters of the metabolic syndrome as described by the IDF, the diagnosis conditions were found for a total of 29 patients of the 156 (18,58%) patients studied during the two years; to note that out of these 29 patients with metabolic syndrome 3 patients (two males and a woman) totaling 10.34% were hospitalized at Railway Clinical Hospital of Craiova for both years of study and that although they registered variations in the values of the parameters used for the diagnosis of the metabolic syndrome for each of the two admissions, the diagnosis was kept.

Studying the 29 patients diagnosed with metabolic syndrome, we found that the gender ratio (M/F) was 1,41 – with 17 men (58,6%) and 12 women (41,4%) (*Figure 5*).

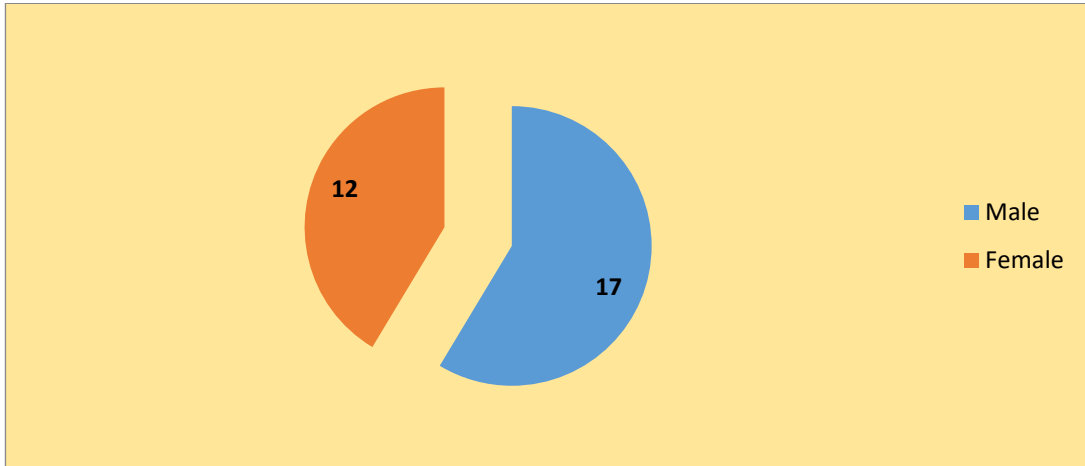


Figure 5. Distribution of patients with metabolic syndrome by sex

The distribution of patients diagnosed with metabolic syndrome according to residence area concluded that 20 patients (68,97%) were form urban areas while 9 patients (31,03%) were from rural areas (Figure 6). This can be explained also explained by the fact that the presence and influence of etiopathogenic factors is higher in urbean areas (fast food consumption, smoking habits, workplace with psychic demand, etc.).

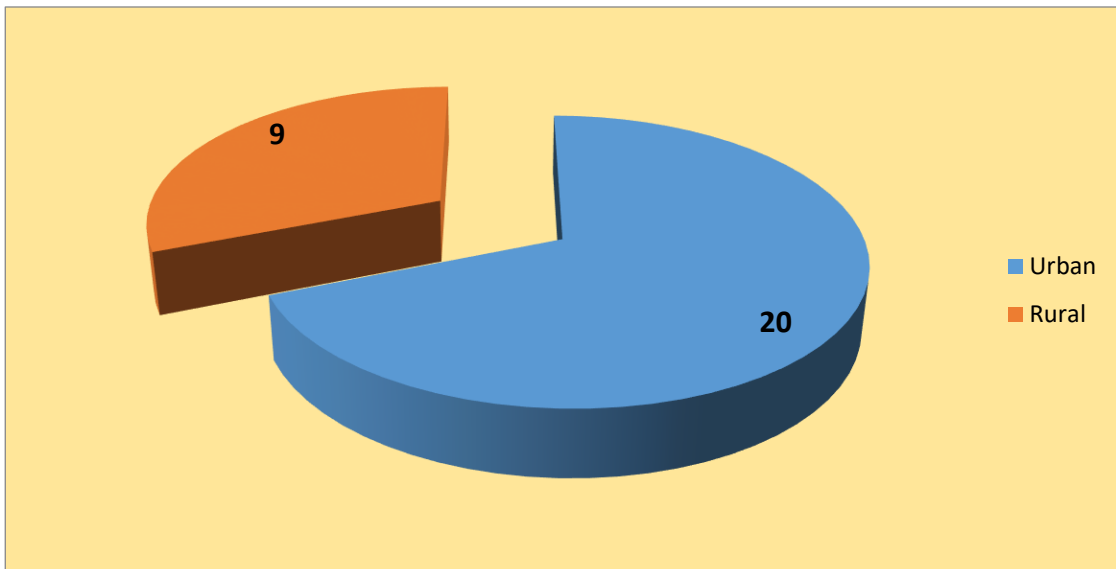


Figure 6. Distribution of patients with metabolic syndrome by residence area

From other anamnestic data collected from the observation sheets, a series of information has been gathered that allowed a lifestyle habits analysis in patients diagnosed with metabolic

syndrome. Thus, regarding alcohol and tobacco consumption, 18 patients (62,06%) declared to use tobacco products while 11 patients (37,93%) are chronic alcohol consumers (*Figure 7*).

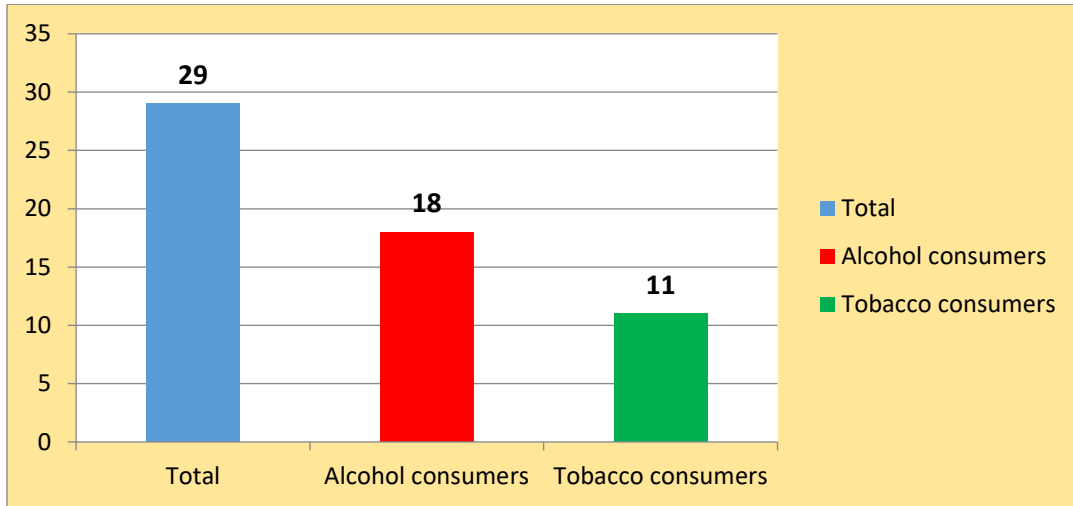


Figure 7. Alcohol and tobacco consumption among metabolic syndrome patients

Unhealthy eating habits – such as high fat consumption or disordered meals – were found in 17 patients (58,62%), while 10 patients (34,48%) declared that their workplace is one with an intense psychic demand (*Figure 8*).

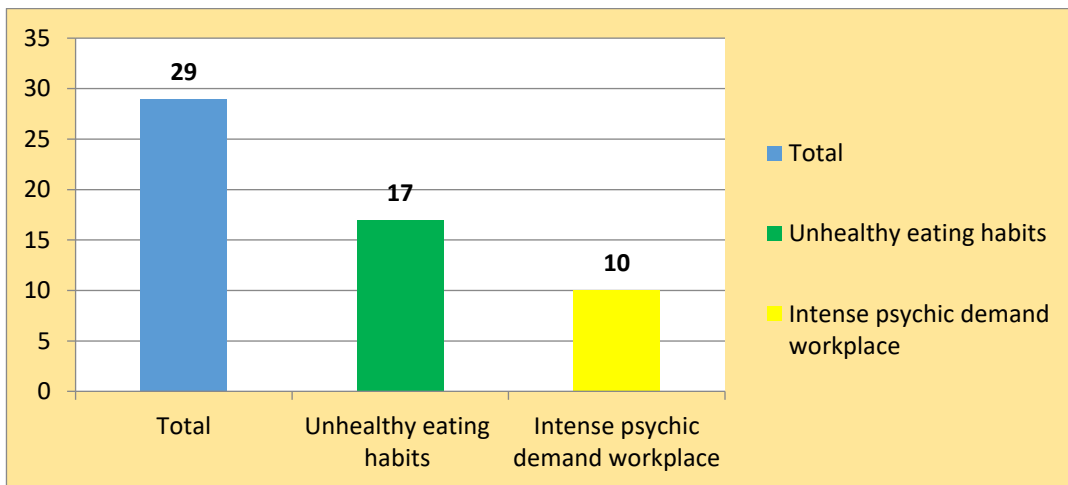


Figure 8. Unhealthy eating habits and psychic demand among metabolic syndrome patients

IV. CONCLUSIONS AND DISCUSSIONS

1. The prevalence of metabolic syndrome for the conducted study was 18,58%, which is similarly to other literature data.
2. The prevalence of metabolic syndrome is not much higher in male patients, this being explained by the fact that the presence and influence of etiopathogenic factors is relatively similar in both sexes.
3. Like other literature data, our study show that lifestyle habits play a fundamental role in the occurrence of metabolic syndrome, and one important role in preventing the onset of metabolic syndrome is the adoption of a healthier lifestyle.

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All authors equally contributed in the research and drafting of this paper.
All authors report no potential conflict of interest.

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THE ASSOCIATION OF ETIOLOGICAL FACTORS IN CHRONIC GASTRITIS

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ABSTRACT

CHRONIC GASTRITIS IS UNDERRATED AROUND THE WORLD, EVEN THOUGH IT'S COMPLICATIONS MAY BE LIFE THREATENING. WITH TIME, THE AGGRESSIVE INFLAMMATION OF STOMACH MUCOSA IN LONG-TERM GASTRITIS CAUSES ATROPHIC GASTRITIS WITH ACID-FREE STOMACH WHICH IS ONE OF THE HIGHEST RISK FACTOR FOR GASTRIC CANCER. OTHER COMPLICATIONS OF CHRONIC GASTRITIS ARE PEPTIC ULCER, BLEEDING ULCER, ANEMIA, FAILURES IN ABSORPTION OF VITAMIN B12 OR NUTRIENTS(IRON, CALCIUM, OR MAGNESIUM).

HELICOBACTER PYLORI - FIRST DISCOVERED IN 1982- IS WELL KNOWN AS THE PRIMARY CAUSE OF CHRONIC GASTRITIS WORLDWIDE.

KEYWORDS: CHRONIC GASTRITIS, HELICOBACTER PYLORI, GASTRIC ULCER, GASTRIC CANCER.

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INTRODUCTION

Chronic gastritis is one of the most common and serious digestive tract disorders characterized by an insidious evolution with severe complications such as gastric ulcer and gastric neoplasm. The notion of chronic gastritis began to be studied a long time ago when Vilardell described for the first time in 1771 the notion of gastritis⁸, but only in 1982 was given more attention with the discovery of the gram negative bacillus by Warren and Marshall⁹.

The prevalence of *Helicobacter pylori* infection varies greatly depending on the socio-economic status, being over 60% in developing countries and with values somewhere between 20-25% in developed countries.¹⁰

MAIN TEXT

AIM OF THE STUDY

In this study we have tried to provide a better understanding and knowledge in chronic gastritis by identifying the incidence and the association of etiological factors in the occurrence of chronic gastritis in 76 patients treated in the Medical Clinic I of the County Clinical Emergency Hospital of Craiova between September 2017 and March 2018.

MATERIAL AND METHODS

The present study was a descriptive study involving 76 patients admitted to the Medical Clinic I of the County Clinical Emergency Hospital of Craiova between September 2017 and March 2018.

The study was conducted in accordance with the ethical and deontological principles of the Helsinki Declaration of Human Rights approved by the local ethics committee and all patients signed an informed consent.

Patient assessment included demographic variables (age, gender, residence area, weight, height, body mass index, personal physiological history). In addition, they were given a questionnaire (*Table 1*) which includes a number of factors known to favor the occurrence of chronic gastritis: eating habits, alcohol consumption, smoking, coffee consumption, chronically non-steroidal anti-inflammatory use, mental stress.

In order to evaluate chronic gastric lesions, the patients included in the study were performed gastroduodenoscopy with gastric mucosa sampling for *Helicobacter pylori* infection detection using rapid urease test.

⁸ Boerhaave. Ventrikuli Inflammatio. In: Van Sweiten, ed Commentaria, 1771 (cited by Vilardell);

⁹ Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulcerations. Lancet 1984; 323: 1311-15.

¹⁰ Bruce MG, Maaroos HI. Epidemiology of Helicobacter pylori infection. Helicobacter. 2008 Oct; 13 Suppl 1:1-6.

EATING HABITS						
	YES			NOT		
Does your diet contain 3 meals a day and do you generally respect their timetable?						
Do you usually eat in the evening after 8 pm and in a larger amount?						
LIFESTYLE AND BEHAVIOR						
Do you frequently drink alcohol? (>3 days/week)						
Do you drink coffee? (>3days/week)						
Do you smoke?						
Do you usually use anti-inflammatory medication? (>7day/month)						
The environment in which you work is an environment with intense psychic demand? (0 - Easy psychic request; 5- Very intense psychic demand)	0	1	2	3	4	5

Table 1. Self-administered questionnaire

RESULTS

Demographics data showed that the age limits were 21 years and 68 years respectively, with a more pronounced distribution over the age range of the third and fifth decade of life (33-55 years). (Figure 1).

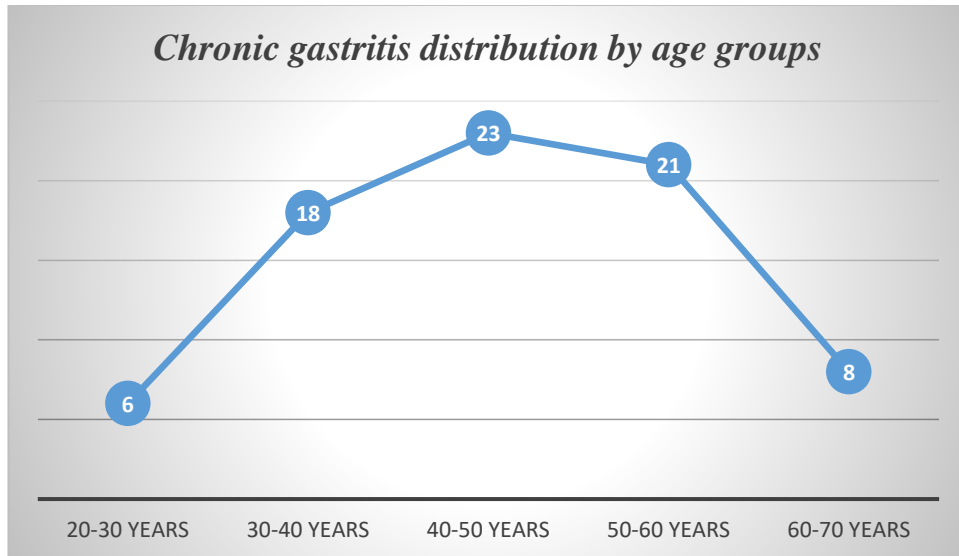


Figure 1. Chronic gastritis distribution by age groups

Regarding gender distribution within the patients group, we found no significant differences. Thus, the gender ratio (female / male ratio) was 0.9, with 40 (52.63%) men, compared with 36 (47.46%) women. (Figure 2).

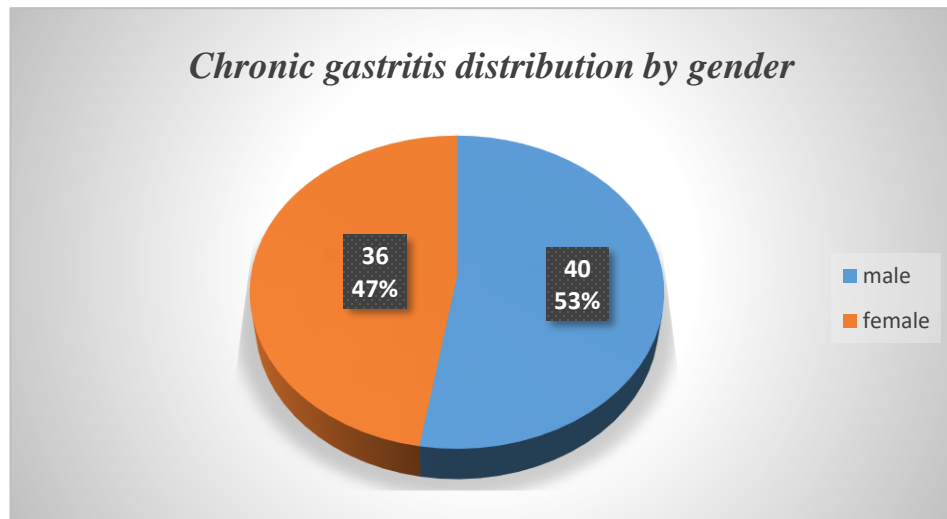


Figure 2. Chronic gastritis distribution by gender

Distribution of patients enrolled in the study by residence area shows a higher share for urban area (53, 69.73%) than the rural one (23, 30.26%). (Figure 3)

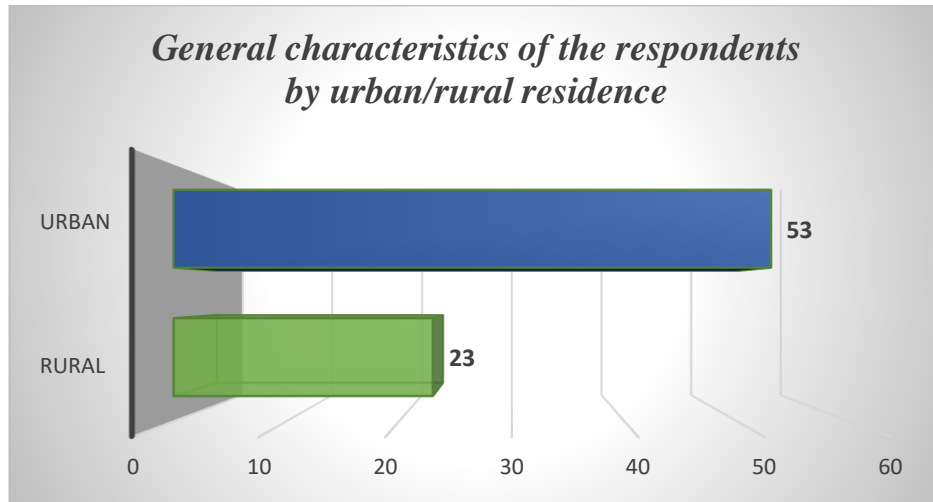


Figure 3. General characteristics of the respondents by urban/rural residence

The importance of *Helicobacter pylori* infection in the occurrence of chronic gastritis is well-known. The results of this study are consistent with similar data from the literature. Thus, following the rapid urease test, 43 patients (56,76%) were found to have *Helicobacter pylori* infection.

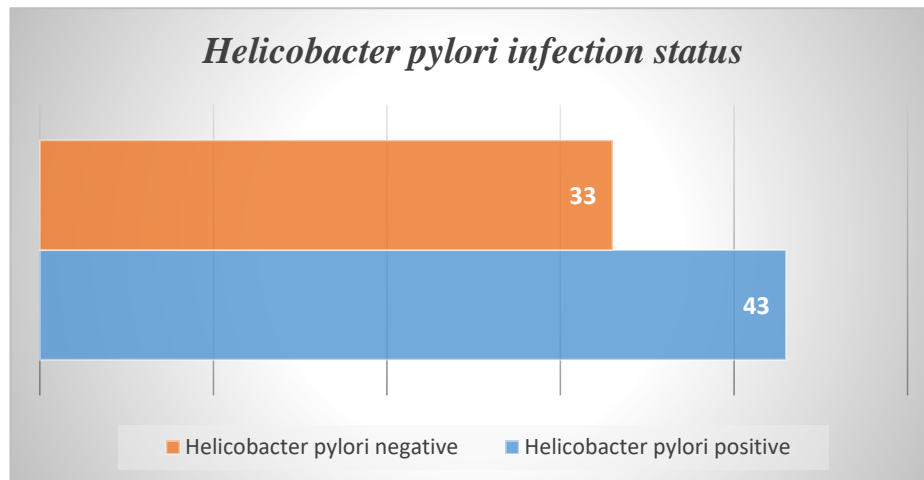


Figure 4. Helicobacter pylori infection status

The results of the self-administered questionnaire analysis presented in the table below (Table 2)(Figure 5) show an increased incidence of unhealthy eating habits (non-observance of meals schedule or food consumption especially during the evening hours) (Figure 6). Thus, 66 patients (86.84%) said they do not have a balanced diet in terms of regimented eating schedule or food consumption after 8pm. Among them, *Helicobacter pylori* infection was found in 40 patients

(52.63% of the total number of patients enrolled in the study, respectively 60.6% of patients with unhealthy eating habits). (Figure 7)

EATING HABITS		
	YES	NOT
Unhealthy eating habits	66	10
LIFESTYLE AND BEHAVIOR		
Chronic alcohol consumers	46	30
Coffee drinkers	59	17
Smokers	48	28
NSAIDs consumers	52	24
Patients who described an intense stress exposure	49	27

Table 2. The results of the self-administered questionnaire

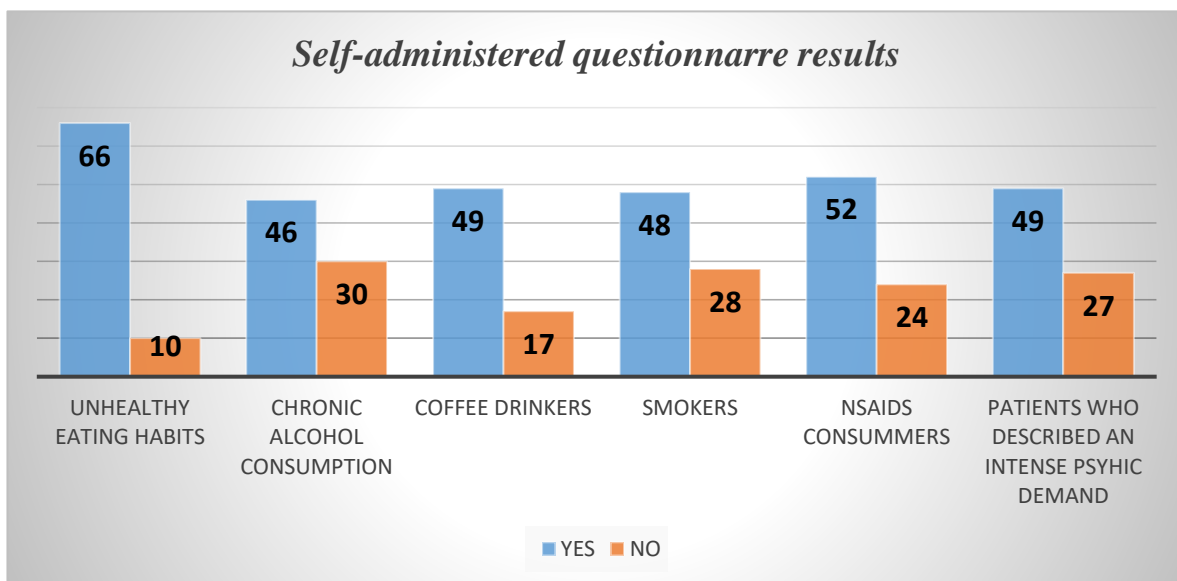


Figure 5. Self administered questionnaire results

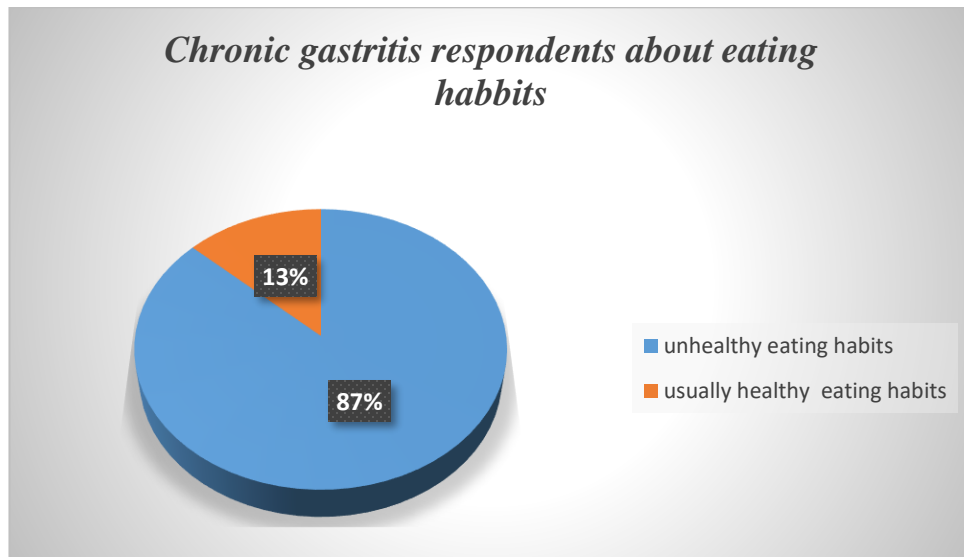


Figure 6.. Chronic gastritis respondents about eating habits

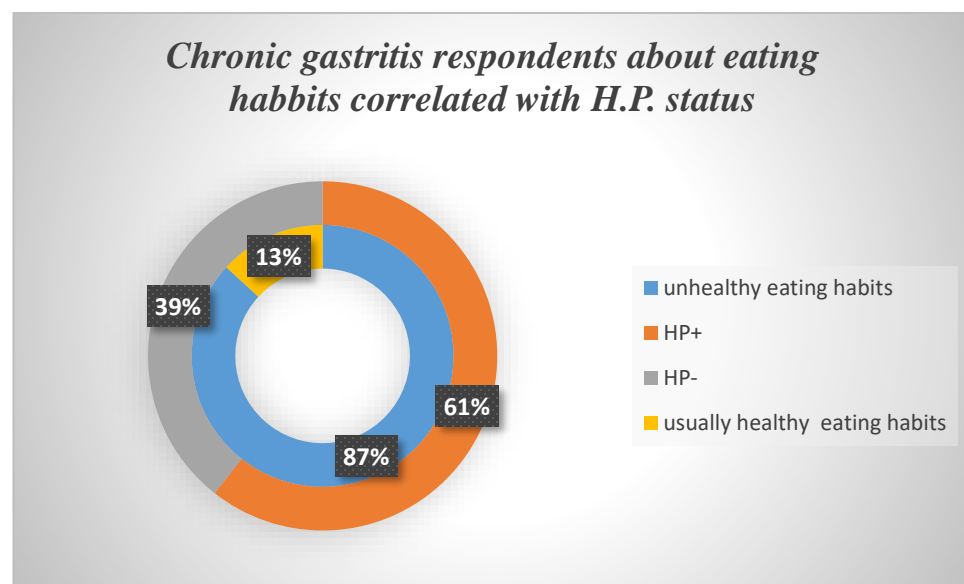


Figure 7. Chronic gastritis respondents about eating habits correlated with H.P. status

Regarding alcohol consumption, 46 patients (60.52%) declared alcohol consumption more than 3 times / week, compared to 30 patients (39.48%) who do not frequently consume alcohol. (Figure 8). Among respondents who frequently drink alcohol, *Helicobacter pylori* infection was found in 31 patients (40.79% of the total patients enrolled in the study, respectively 67.39% of the chronic drinkers). (Figure 9)

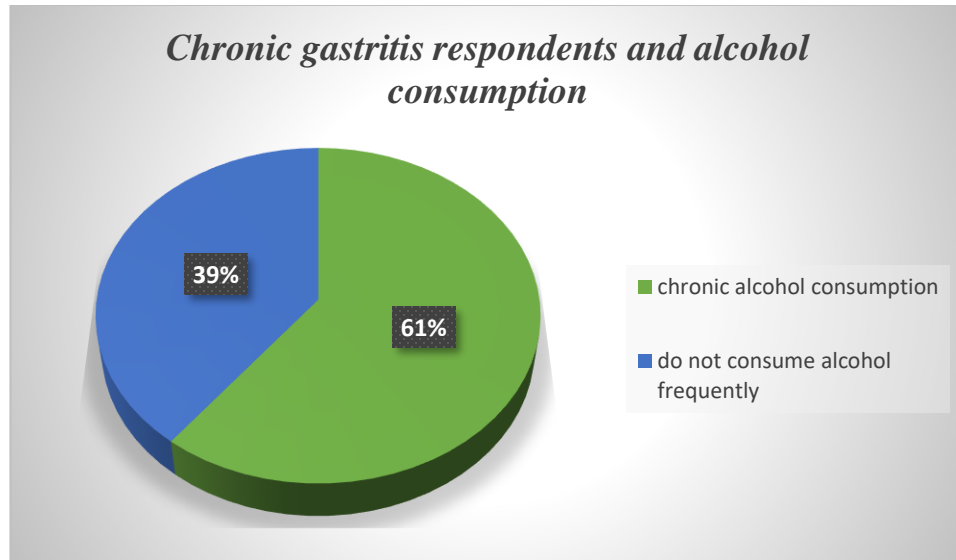


Figure 8. Chronic gastritis respondents about alcohol consumption

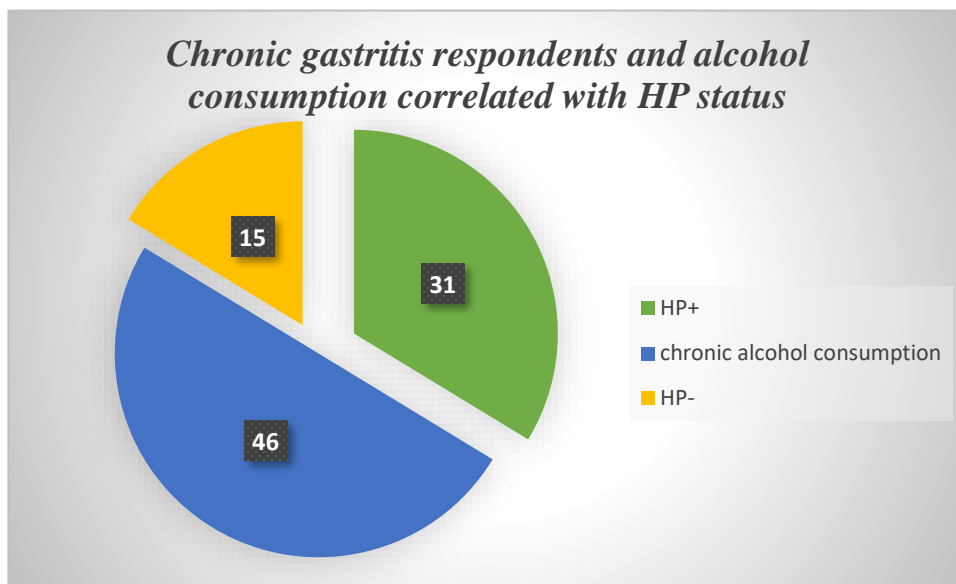


Figure 9. Chronic gastritis respondents and alcohol consumption correlated with HP status

In terms of coffee consumption, 59 respondents reported frequent coffee consumption, accounting for 77.63% of the total number of patients included in the study (Figure 10). Among the coffee users in the studied group, the number of patients who experienced *Helicobacter pylori* infection (28, 47.45%) was similar to those in whom the rapid urease test was negative (52.55%). (Figure 11)

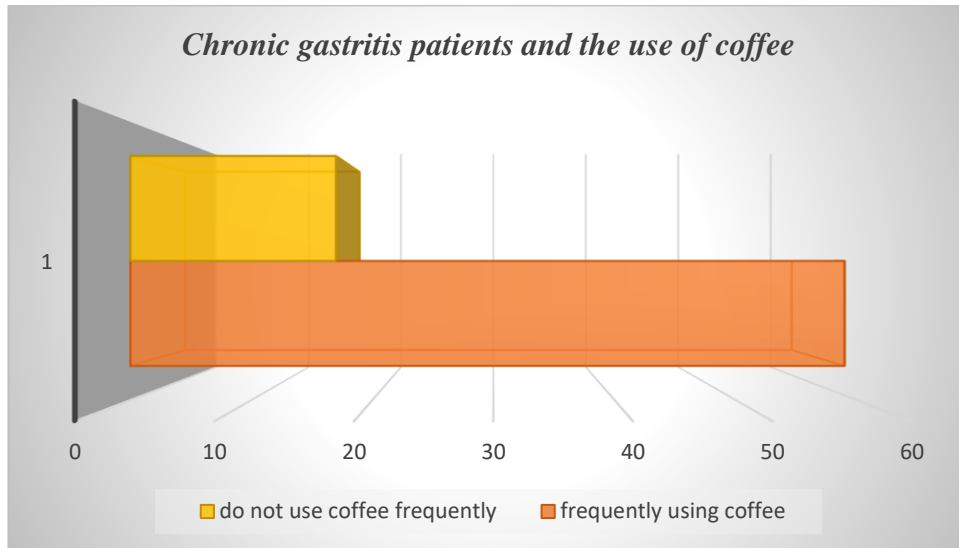


Figure 10. The use of coffee among chronic gastritis patients

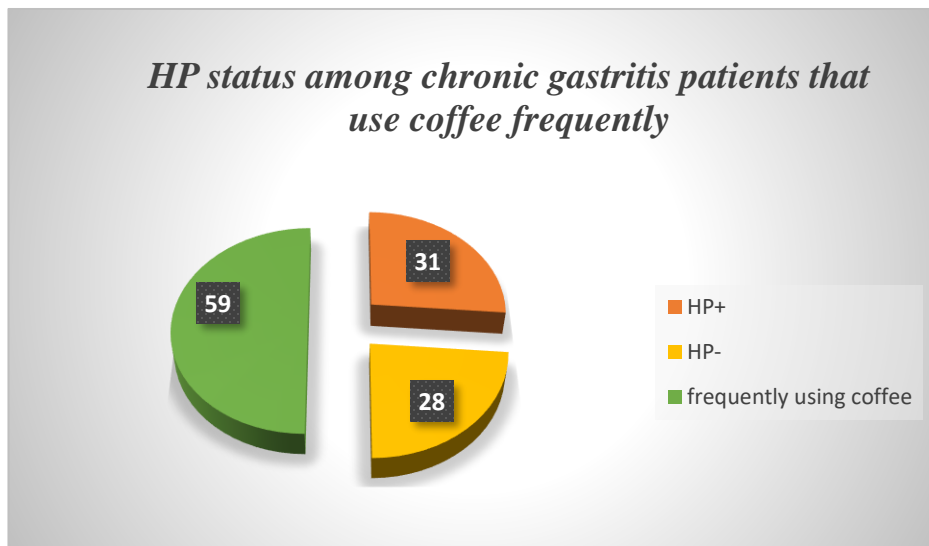


Figure 11. H.P. status among coffee users with chronic gastritis

In the case of smokers - 48 (63.16%) (Figure 12) - a large proportion of them - 34 (44.73% of the total number of patients included in the study, respectively 70.83% of the total who were declared smokers) also had *Helicobacter pylori* infection (Figure 13).

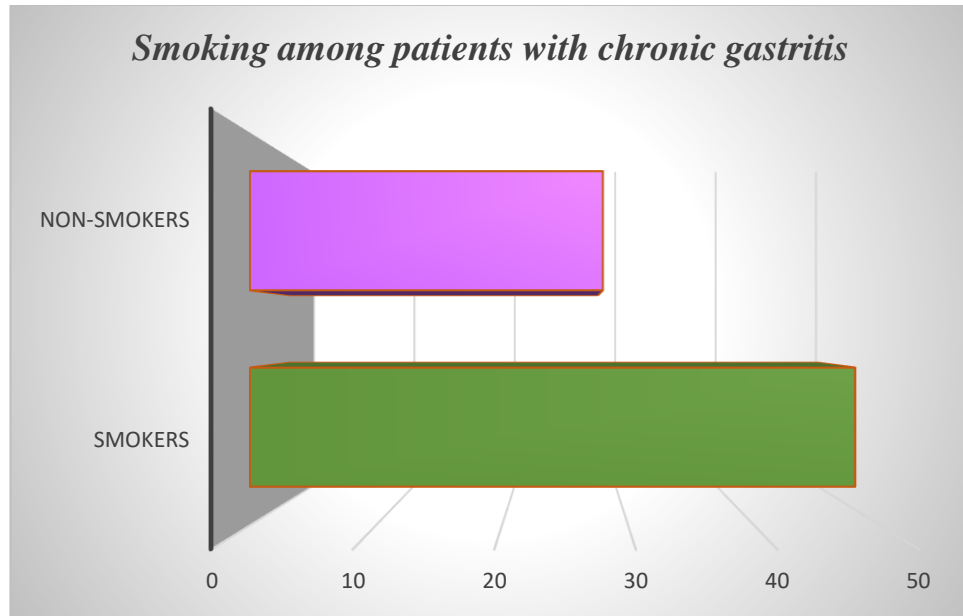


Figure 12. Smoking habit among patients with chronic gastritis

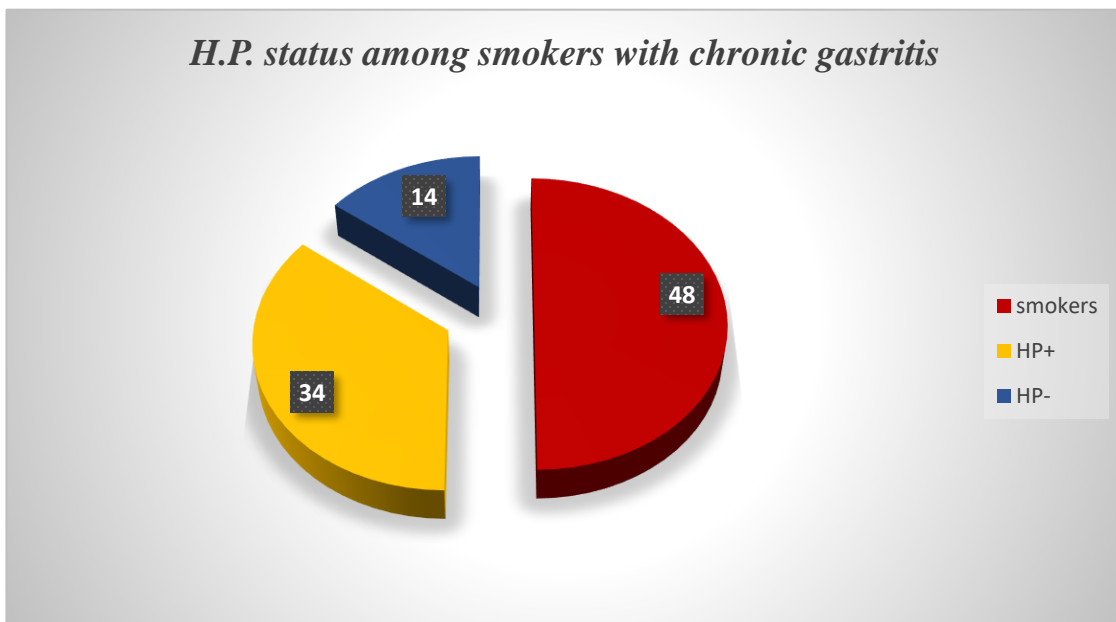


Figure 13. HP status among smokers with chronic gastritis

Regarding the consumption of non-steroidal anti-inflammatory drugs, 52 patients (68.42%) reported their frequent consumption. (Figure 14). Among them there were no significant differences between patients who had *Helicobacter pylori* infection - 24 (46, 15%) and those in whom urease fast test was negative -28 (53.85%) (Figure 15)

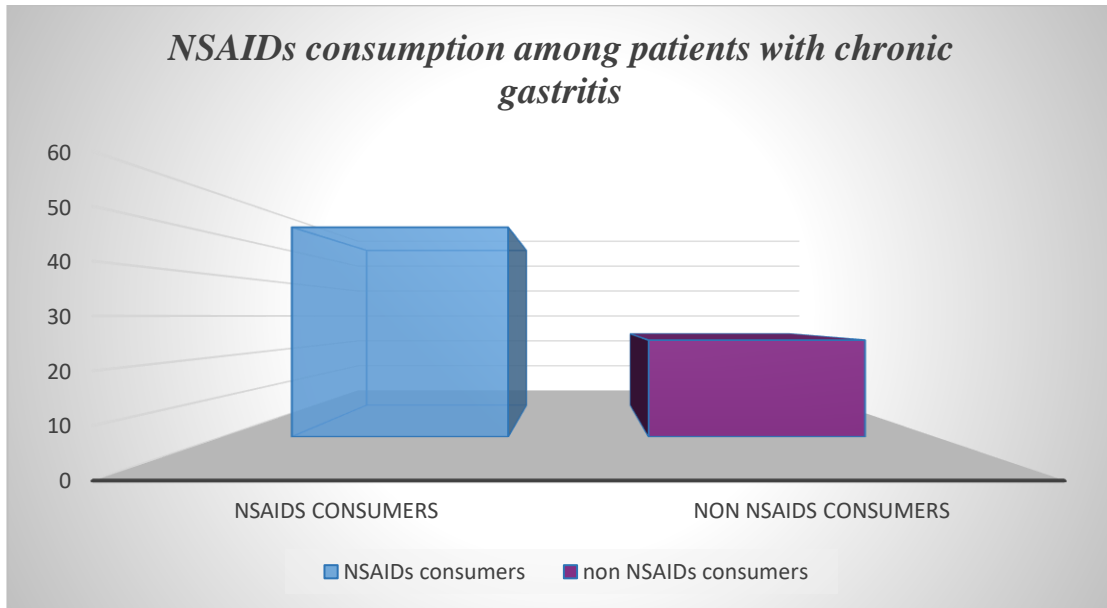


Figure 14. NSAIDs consumption among patients with chronic gastritis

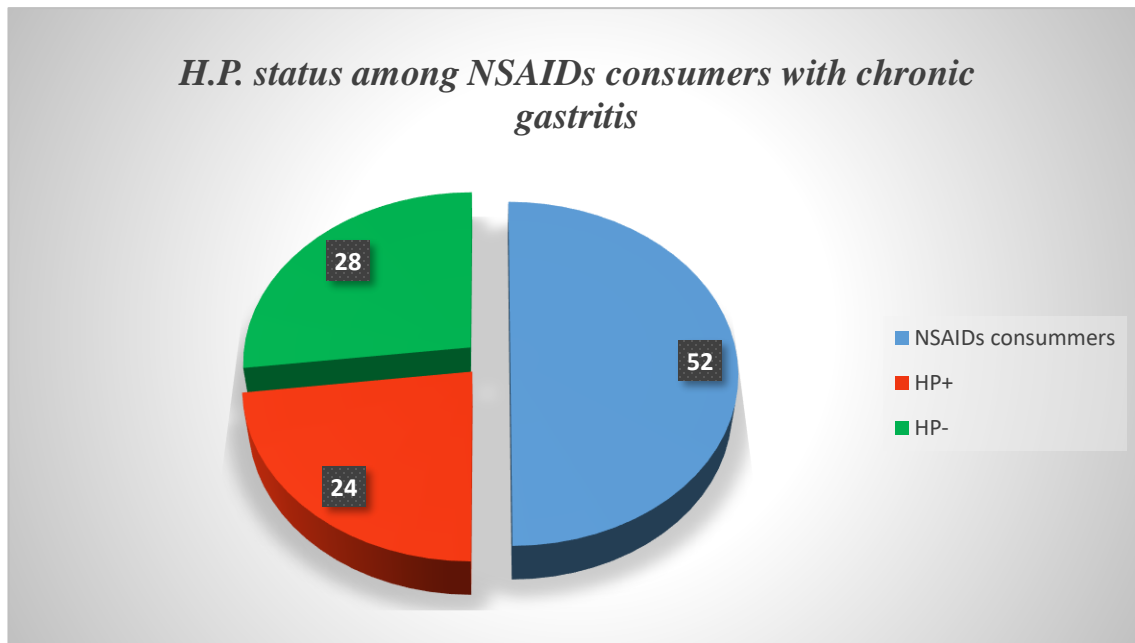


Figure 15. H.P. status among NSAIDs consumers with chronic gastritis

Regarding the psychological solicitation of patients due to the environment in which they work, 49 respondents (64,47%) declared that the environment in which they operate is quite psychological intense (corresponding to the values 3,4 and 5 of the questionnaire) (Figure 16). Of these, *Helicobacter pylori* infection was detected in a total of 35 patients, representing 46.05% of

the total number of patients enrolled in the study, respectively 71.42% of the number of respondents who are working in a stress exposed environment (*Figure 17*).

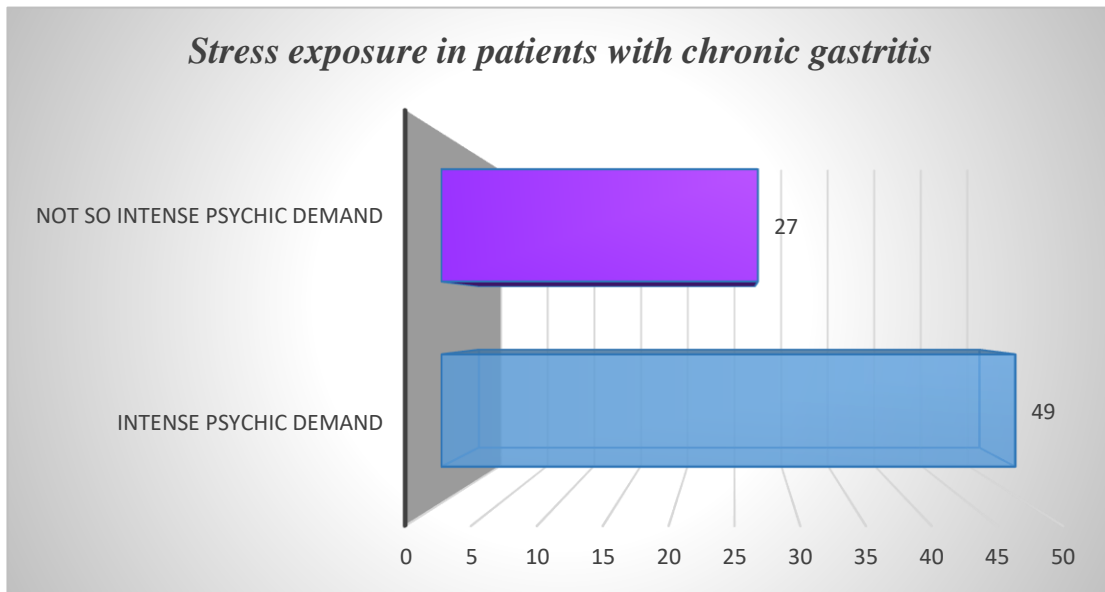


Figure 16. Stress exposure among patients with chronic gastritis

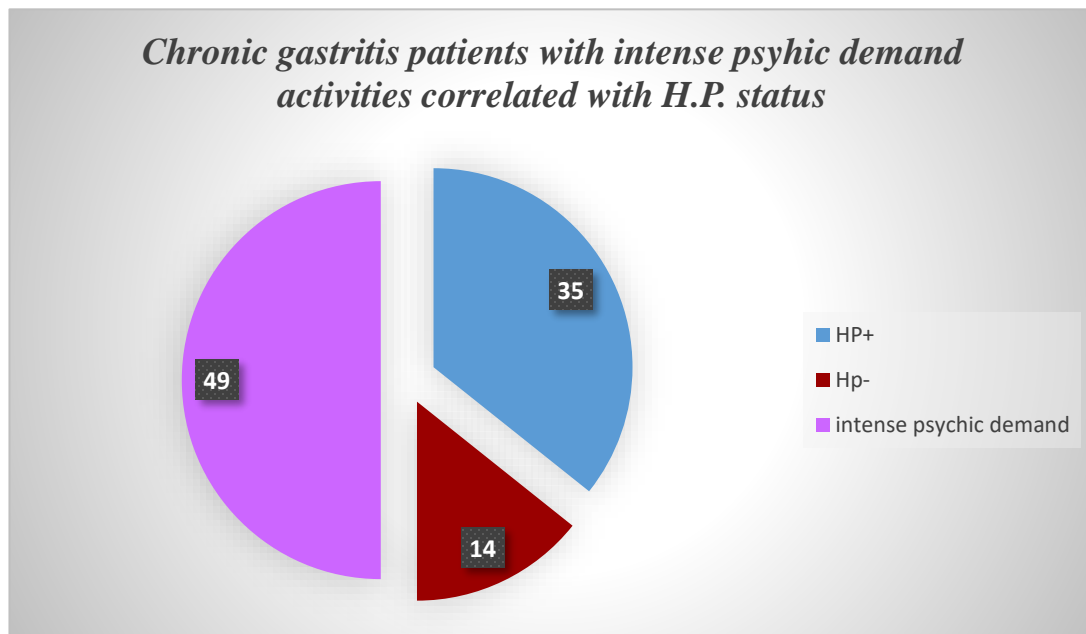


Figure 17 Hp. Status in chronic gastritis patients with intense psychic demand activities

DISCUSSIONS AND CONCLUSIONS

The results of the presented study are similar to those presented in medical literature. We observed an increased incidence of *Helicobacter pylori* infection in patients with chronic gastritis - again proving its role in the etiopathogeny of chronic gastritis.

Analysis of demographic data in this study shows an increased incidence of chronic gastritis within the active age range (30-60 years), which is explained by a more pronounced influence of the etiological factors of chronic gastritis (especially unhealthy eating habits, psychological solicitation, drinking alcohol, coffee and smoking) over the above mentioned age range.

At the same time, gender distribution of patients without significant differences is similar to that present in the medical literature and can be explained by the fact that the presence and influence of etiopathogenic factors is relatively similar in both sexes.

Regarding the distribution of patients by residence area, the greater share of urban patients can be explained both by the presence of a more stressful lifestyle and by the increased accessibility of urban patients to services medical, but also a better medical education, which causes them to present themselves to the doctor when the symptoms appear.

ACKNOWLEDGEMENTS

All authors equally contributed in the research and drafting of this paper.

All authors report no potential conflict of interest.

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NATURAL SUPPLEMENTS CONSUMPTION AMONG MEDICAL STUDENTS

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ABSTRACT

THE CATEGORY OF NATURAL SUPPLEMENTS INCLUDE A WIDE RANGE OF PRODUCTS FROM SIMPLE VITAMINS, MINERALS, VITAMIN AND MINERAL COMPLEXES TO COMPLEX FORMULAS OF SUBSTANCES WITH NUTRITIONAL OR PHYSICAL EFFECT.

RELATIVELY RECENTLY INTRODUCED, THE „NATURAL SUPPLEMENT” CONCEPT BEGAN TO GROW EXPANSIVELY IN RECENT YEARS, ON THE ONE SIDE BECAUSE OF THE MEDIA DIRECTLY INVOLVED IN PROMOTING THESE PRODUCTS AND ON THE OTHER SIDE BECAUSE OF THE INCREASINGLY POLLUTING ENVIRONMENT THAT CAN INDUCE A MORE PRECARIOUS STATE OF HEALTH AND A LIFE-STYLE WITH THE SPECIFIC DAILY STRESS SINCE THE END OF THE TWENTIETH CENTURY INVOLVED IN THE INCREASED PREVALENCE OF MANY DISEASES.

IN 2017, THE RENOWNED PERSISTENCE RESEARCH MARKET (PMR) ANNOUNCED A MARKET SURVEY SHOWING THAT IN 2016 THE GLOBAL NATURAL HEALTH SUPPLEMENTS MARKET VALUE WAS ABOUT 37 BILLION US DOLLARS AND BY THE END OF 2024 THE FIGURE IS EXPECTED TO REACH ABOUT 70 BILLION US DOLLARS.⁷

KEYWORDS: NATURAL SUPPLEMENTS, NUTRITION, HEALTH, MEDIA

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⁷ Persistence Market Research, “Global Market Study on Natural Health Supplements: Marine Segment by Source Expected to Remain Dominant in Terms of Value During 2016-2024”, report published on April 2017

INTRODUCTION

In recent years, as in other EU countries, there has been a significant increase in the consumption of natural supplements by different population groups, in the face of an increasingly alert lifestyle and the desire of improving or maintaining an optimal health condition, all of this given that the attention paid to a sanogenic diet has increasingly reduced.¹

Increasing use of natural supplements is closely correlated with self-management of common health problems, which only very little, unfortunately, involves the advice or recommendation of specialized healthcare professionals.

The spectacular evolution of the natural supplements market (according to Cegedim data, sales of vitamins and natural supplements had a market share of 21.1% of all non-prescription medicines in the last three months of 2017²) are largely due to aggressive promotion of the benefits of using this type of product on most of communication channels (TV advertisements, press editorial, teleshopping for food supplements, extensive internet promotion, etc.).

Essentially, however, dietary supplements are products designed to provide a supply that is closest to the human body's needs of some nutritional deficiencies in the current unbalanced diet; under no circumstances may their use be more than just a "damage" measure in certain specific situations, and not a substitute for a sufficient and varied diet.

The main regulation in force regarding food supplements in the legislation in Romania is represented by the Order of the Ministry of Health no. 1069/2007 approving the Norms on Food Supplements, Order transposing the EU Directive no. 2002/46 / EC.

However, the risks of long-term administration of dietary supplements have to be taken into consideration, namely that it can be correlated with the accumulation of biochemical compounds that may cause liver or kidney toxicity. Also, it should not be minimized the possible interaction of compounds in natural supplements with other drugs.

MAIN TEXT

I. THE AIM OF THE STUDY

In the context of the above, the present study aims to identify the behavior of medical students of University of Medicine and Pharmacy of Craiova in relation to natural supplements, the ways of choosing a food supplement and the conditions in which they are consumed. Also, in the course of this study it has not been minimized the investigation of students' medical knowledge regarding the different groups of nutrients and the applicability of accumulated knowledge in the educational process in substantiating recommendations for the use of natural supplements by their future patients.

II. MATERIAL AND METHOD

The conducted study was a retrospective descriptive study based on an individual anonymous questionnaire of 213 fourth year students from the University of Medicine and Pharmacy of Craiova; the study was conducted between October 2017 and May 2018.

¹ Ministry of Health – Public Health National Institute „Natural Supplements - guide”– Garban G., Florescu N., Bucharest 2013

² Cegedim Romania, “Pharma & Hospital Report Study”, published on 8th of February 2018

The individual questionnaire was structured into two segments of information: the first of these segments, containing a total of 9 questions, was centered on students' attitudes towards the personal use of the natural supplements, and the second segment brought together nine other questions the possibility of undesirable and / or unpleasant effects of dietary supplements, and the general considerations of recommending their use to patients.

III. RESULTS AND DISCUSSIONS

The results of the study as shown in *Table 1*, show that more than half of the respondents (68.54%, 146 people) used dietary supplements; the gender distribution of consumers of such products shows a greater agglomeration of female users (92 female users, accounting for 70.76% of female participants in the study, respectively 63% of the total number of consumers). By comparison, only 54 male users (representing 65.06% of male participants in the study, respectively 37% of the total number of consumers) used such products. (*Figure 1*).

Question	Possible responses	Responders	(%)
Did you use natural supplements ?	Yes	146	68,54%
	No	70	31.46%
For how long did you use natural supplements?	<i>Less than one month</i>		
	<i>Between 1and 3 months</i>	38	26,00%
	<i>More than 3 months</i>	52	35.61%
What type of dietary supplements did you use?	<i>Vitamins</i>	56	38.39%
	<i>Minerals(</i>	34	23,28%
	<i>Complexes of vitamins and mnerals</i>	26	17,81%
		86	58.90%

Did you noticed any significant improvement of physical or intellectual performance?	Yes	114	78,08%
	No	32	21,91%
Did you interrupt the administration of dietary supplements because of some unwanted side effects?	Yes	6	4,11%
	No	140	95,89%
The use of natural supplements took place during exhausting periods?	No	16	10,97%
	Yes, during intense intellectual efforts periods	23	15,75%
	Yes, during intense physical efforts periods	107	73,28%
Did you noticed any adjustments regarding diet and food intake during the period you consumed natural supplements?	No	122	83,56%
	Yes, I reduced the food intake	11	7,53%
	Yes, I supplemented the food intake	13	8,91%

Did natural supplements intake had any effects on your weight?	No	100	68,49%
	Yes, I had weight gain	26	17,80%
	Yes, I had weight loss	20	13,71%

Table 1. The results of the self-administered questionnaire – first segment

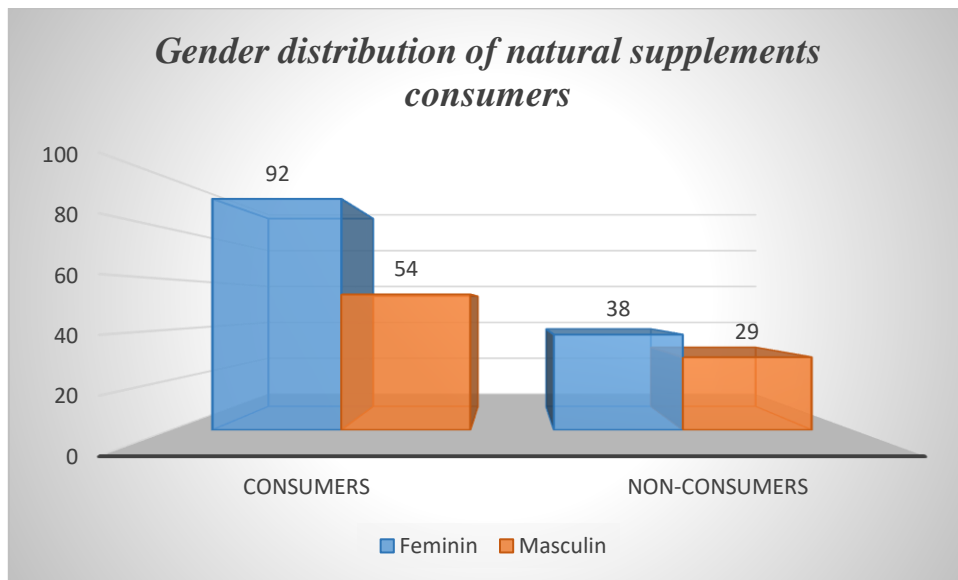


Figure 1. Gender distribution of natural supplements consumers

Regarding the duration of the self-administration of natural supplements, the majority of respondents (61.64%, 90) used such products for a period of less than one month, while a much lower proportion (23.28%, 34) used supplements for more than three months.

The first segment of the questionnaire underlying the present study also brings important data regarding the type of natural supplements used by the respondents: the first place in their preferences was taken by the complexes of vitamins and minerals (58.90%, 86) while the preparations made exclusively from vitamins or minerals only reach 22.38%, (34 people) of preferences for vitamin products and 17.81% respectively, 26 for those made up of different types of mineral elements. (*Figure 2*).

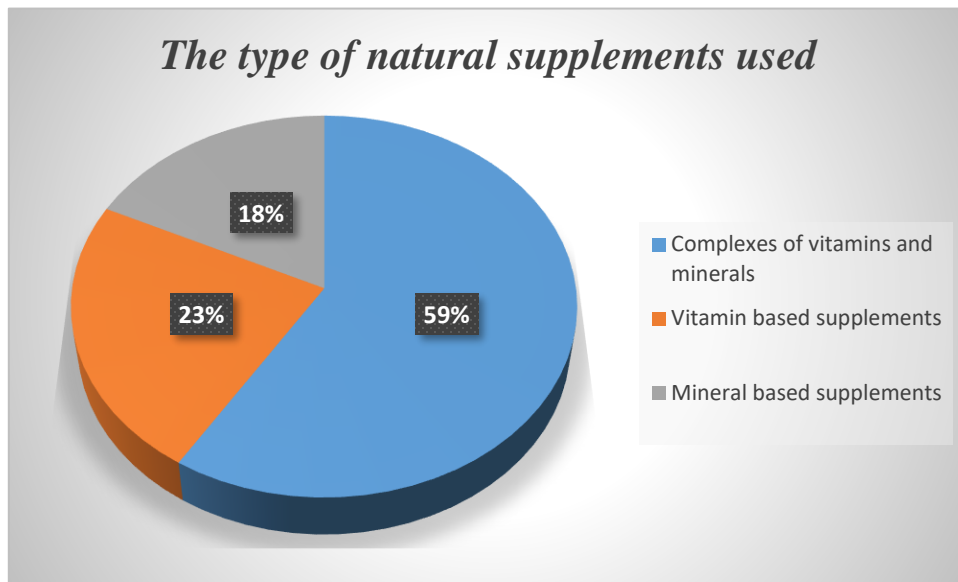


Figure. 2. The type of natural supplements used

Compliance with administration as well as the self-assessment on the effect of natural supplements administration on human health and / or on the physical and intellectual performance of the respondents show that, for the most part (78.08% 114), they found a substantial improvement of physical or intellectual performance compared to only 21.91% (32 people) of respondents who did not notice any significant changes on these parameters (*Figure 3*). The use of natural supplements, according to the answers from the processed questionnaires, seems to be free from interference / negative influences leading to the discontinuation of their administration, a very high proportion (95.89% and 140 of the 146 participants) had no reason to renounce on these products for the during the treatment period.

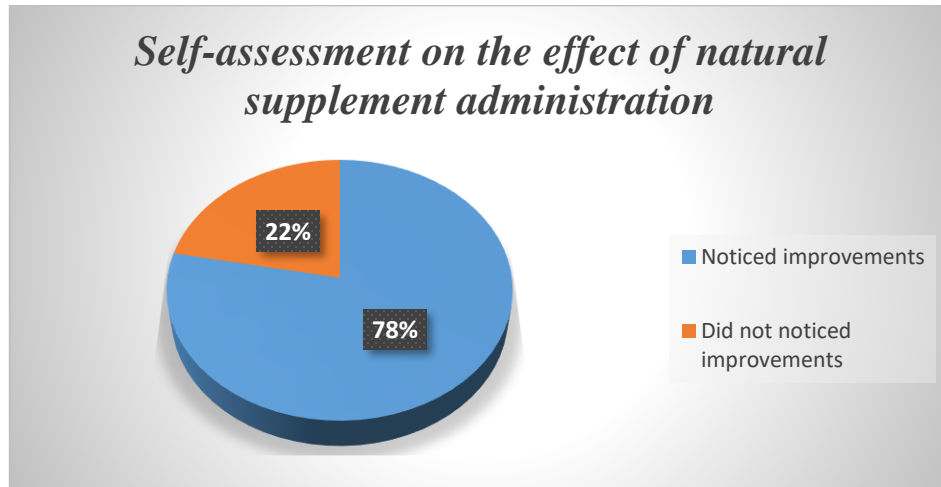


Figure 3. Self-assessment on the effect of natural supplement administration

An important aspect emerging from the thorough analysis of the answers from the first segment of the questionnaire used in this study is that the decision to self-administer natural supplements, regardless of their basic constituents (vitamins, minerals, vitamin complexes and minerals) was often dictated by going through some exhausting periods of physical (43.83%, 64) or intellectual (45.20%, 66) efforts.

The attention of respondents using natural supplements regarding the diet and food intake adjustment over the periods when natural supplements were administered did not in most cases (83.56%, 122) lead to a change in diet; only in small proportions, the consumption of dietary supplements led to a negative (7.53%, 11) or positive (8.91%, 13) adjustment of food intake (Figure 4). However, although most participants in the study (68.49%, 100) found no direct link between the consumption of natural supplements and the weight changes that occurred during the same period, in some cases, the respondents observed weight gain (17,80%, 26) or a weight loss (13,71%, 20) (Figure 5).

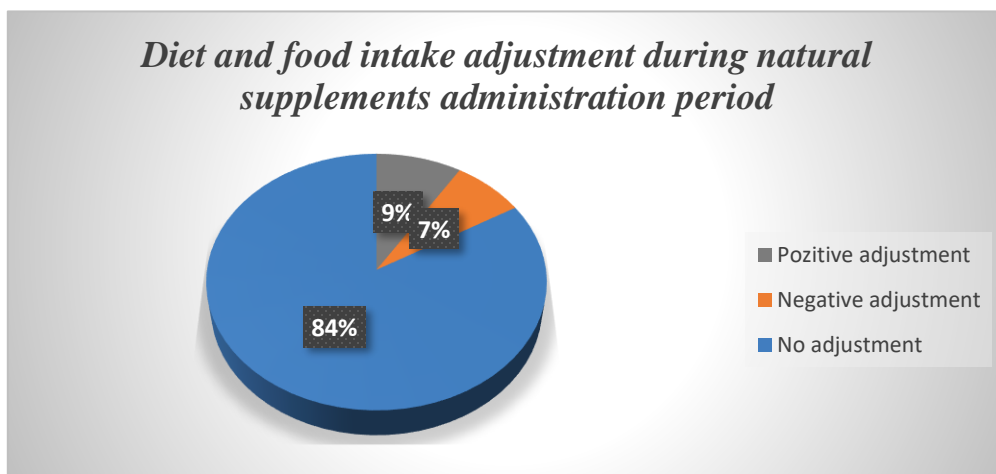


Figure 4. Diet and food intake adjustment during natural supplements administration period

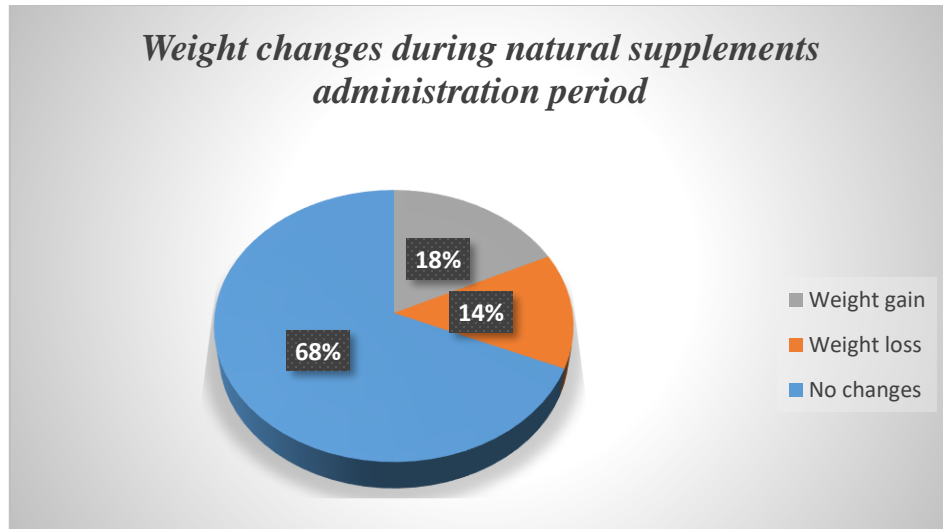


Figure. 5. Weight changes during natural supplements administration period

Corroborating the information outlined above regarding the intention of users to increase or decrease food intake on the one hand with the informations on weight gain or weight loss during the period of dietary supplements administration on the other hand indicates a concern for respondents in terms of optimal weight maintenance.

The second section of the questionnaire used in the present study provides eloquent information upon the degree of awareness of possibility of unwanted / unpleasant effects in case of natural supplements administration, as well as information on the behavior and attitude of future physicians towards recommending these pharmaceuticals to patients. All the information obtained in this second part of the questionnaire required direct links in the elaboration of the responses between the respondents experience regarding the use of natural supplements and the need to approach a future therapeutic course in medical activity (*Table 2*).

Questions	Possible answers	Respondents	(%)
Do you consider the use of natural supplements as a benefit for human health?	Yes	196	92,00%
	No	17	8.00%
Would you recomend natural supplements to your future patients?	Yes	168	78,88%
	No	45	21,12%
In case you would recomend dietary supplements to your patients, would you follow up their health status?	No	200	90,62%
	Yes	13	9,38%
May natural supplements use by your patients influence your future therapeutic approach?	Yes	96	45,07%
	No	79	37.08%
	I do not know	38	17,85%
Do you have knowledge of any interractions between dietary supplements and other drugs	Yes	116	54,46%
	No	97	45,54%

Would you consider a diet adjustment for your future patients in case they use natural supplements?	<i>Yes</i>	188	88,26%
	<i>No</i>	25	11,74%
Did you use natural supplements that were recommended by a medical field qualified person? Or by a nutritionist/dietician?	<i>No</i>	128	87.67%
	<i>Yes, medical personnel</i>	12	8,21%
	<i>Yes, a nutritionist/dietician</i>	6	4,12%
Where did you purchased natural supplements from?	<i>Drogstore/ Pharmacies</i>	119	81,50%
	<i>On-line</i>	26	17,80%
	<i>Other</i>	1	0,68%
Chosing a specific type of supplement was determined by :	<i>Price</i>	78	53,42%
		43	29,45%

	Marketing (commercials)	25	17,13%
	Accesibility		

Table 2 Self- administered questioannaire results – IInd segment

Thus, more than 90% of the people involved in the study (92.00%, 196) consider that the consumption of dietary supplements as being benefic for human health and consequently an equally high proportion (78.88% 168) states that they will recommend to their patients the use of these products (*Figure 6*).

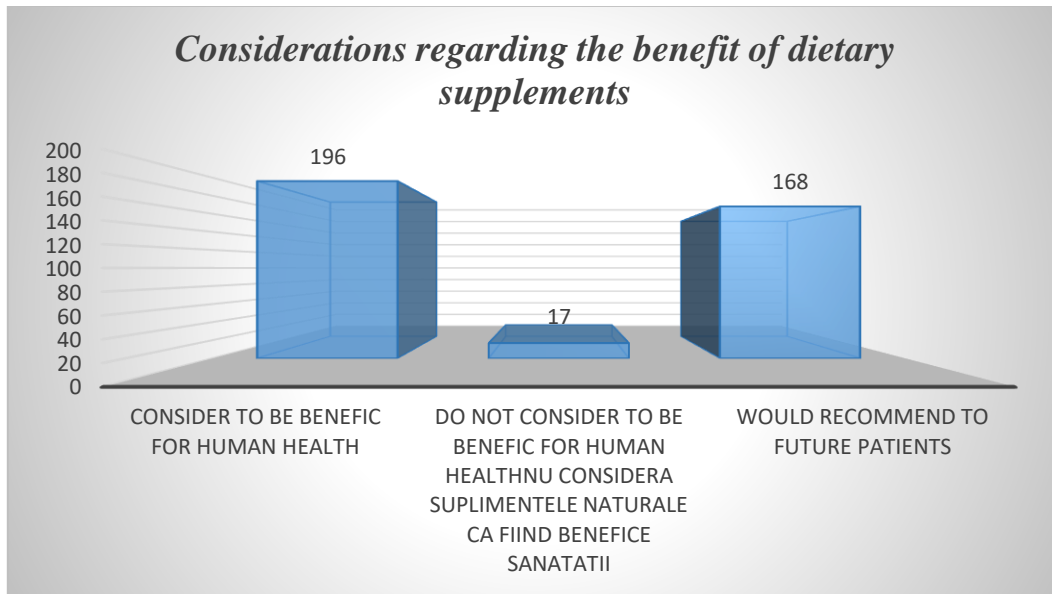


Figure. 6. Considerations regarding the benefit of dietary supplements

The ongoing professional medical training, which does not yet provide them with all the necessary information for the in-depth knowledge of the possible interactions between the pharmacological preparations used in the therapy of various diseases and the constituents of the dietary supplements³, determines similar percentages of positive responses (54,46%, 116)

³ Vlaicu B., 1994, Dynamics of Physical Development and Behavioral Issues in Schools, Signata Ed..

respectively negative (45,54%, 97) when questioning the participants about the incidents that may occur when combining both types – drugs and natural supplements (*Figure 7*).

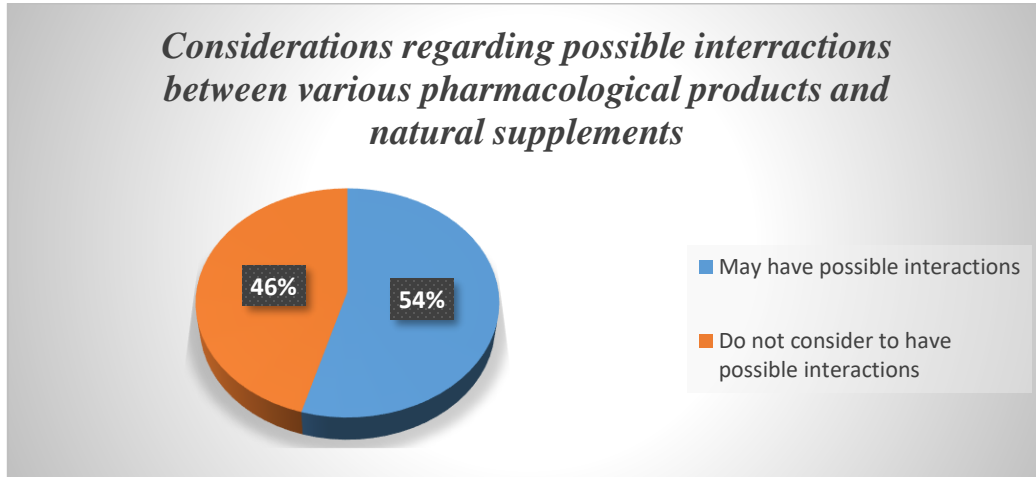


Fig. 7. Considerations regarding possible interactions between various pharmacological products and natural supplements

At the same time, however, it is important to note that the same medical training induces respondents the responsibility of adjusting the daily diet in patients receiving natural supplements (88.26%, 188); however, careful monitoring of the overall therapeutic response in these patients seems not to be a priority for the study participants, less than half (45.07%, 96) considering it necessary to closely monitor the association of simultaneous administration of pharmacological products and natural supplements.

Important in the context of the present study are also the starting points for dietary supplements administration, the access to their purchase and the determinations that have been the basis for choosing a certain type of dietary supplement; the majority of the respondents initiated the use of natural supplements by their own decision (87.67%, 128), without the recommendation or opinion of specialized staff, very little opinion from the medical staff - doctors (8, 21%, 12) or a dietitian (4.12%, 6) (*Figure 8*).

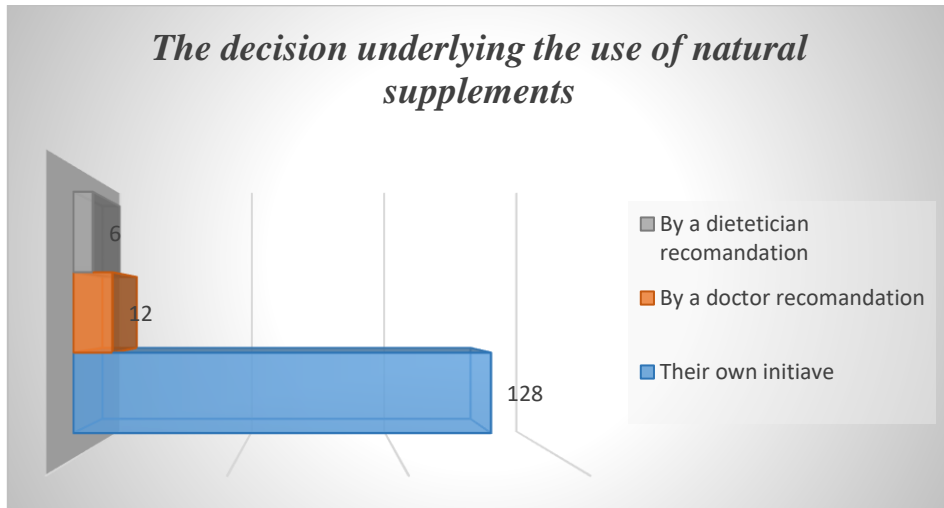


Figure 8. The decision underlying the use of natural supplements

The most used acquisition channel for purchasing natural supplements was represented by pharmacies / drugstores (80.82%, 118); the purchase of natural supplements from the on-line environment was used in a much smaller proportion (19.17%, 28), other purchase methods being insignificant (*Figure 9*).

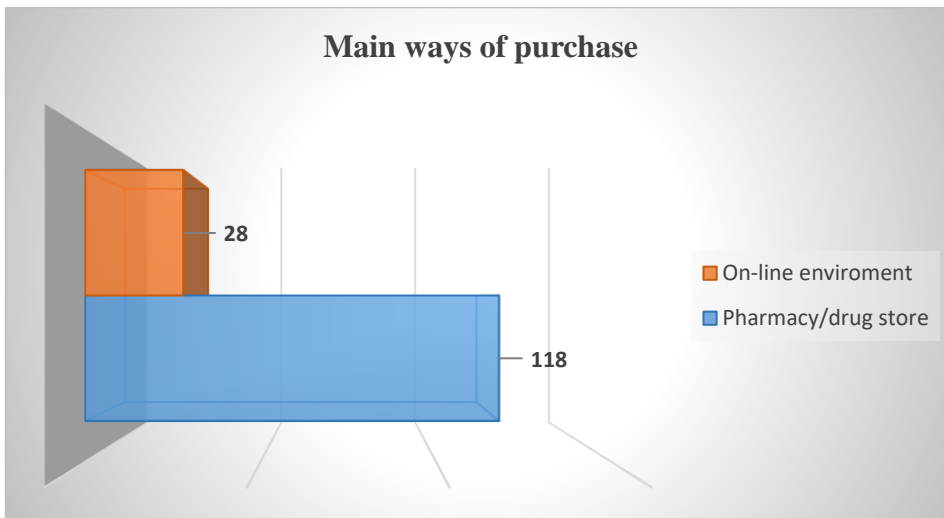


Figure 9. Main ways of purchase

Regarding the criteria underlying the choice of a particular type / brand of dietary supplement, the study participants highlighted cost price (56.16%, 82) as a matter of great importance, followed secondly by actions to promote this type of supplement (TV advertisements, promotions, etc.) (Figure.10).

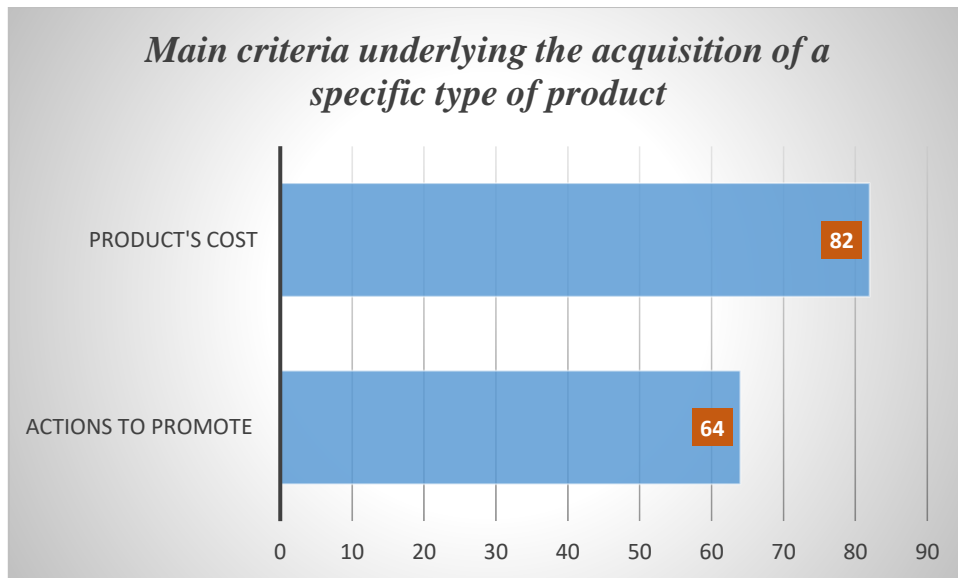


Fig.10. Main criteria underlying the acquisition of a specific type of product

CONCLUSIONS

For the investigated group of respondents we found, on the one hand, the development of a favorable attitude towards the consumption of dietary supplements – based on the belief of their benefit for human health, and on the other hand, a greater attention paid to the deepening the knowledge about these products in the context of future medical practice and the complexity of the medical act.

Although at the time of the study, the consumption of natural supplements of the participants had, in most cases, rather intuitive fundamentals regarding their role in maintaining and improving the health status and the factors that determined the choice of a particular type of supplement were financial related, the willingness of the respondents to deepen the knowledge related to this subject and, together with it, to improve the decision-making process of recommending their consumption by the patients can not be disputed.

Finding an improvement in overall health status determines, in the case of participants in this study, a greater confidence in the management of natural supplements, a confidence that, due to limited knowledge, is not affected at this time by the awareness of all accidents and incidents that may occur as a result of the combination of a drug treatment with the uncontrolled intake of nutritional supplements.

ACKNOWLEDGEMENTS

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All authors report no potential conflict of interest.

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CHOLECYSTITIS- CLINICAL AND THERAPEUTICAL ASPECTS

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ABSTRACT

CHOLECYSTITIS, AN INFLAMMATORY AFFECTION WHICH OCCURS IN MOST CASES AS A COMPLICATION OF THE CHOLELITHIASIS, APPEARS IN TWO FORMS: ACUTE AND CHRONIC. THE SURGICAL APPROACH OF THIS PATHOLOGY EVOLVED CONTINUALLY STARTING WITH THE FIRST CHOLECYSTECTOMY MADE BY LAUGENBUCH IN 1882 UP TO THE LAPAROSCOPIC CHOLECYSTECTOMY INTRODUCED IN 1985 WHICH BECAME" THE GOLDEN STANDARD" OF SURGERIES NOWADAYS. LAPAROSCOPIC CHOLECYSTECTOMY CAN TRIGGER A WHOLE RANGE OF COMPLICATIONS AND TECHNICAL DIFFICULTIES. THE AIM OF THE STUDY IS TO MAKE A RETROSPECTIVE ANALYSIS OF THE TREATMENT APPLIED TO PATIENTS HOSPITALIZED FOR ACUTE AND CHRONIC CHOLELITHIASIS IN THE SURGERY CLINIC OF THE RAILWAY CLINICAL HOSPITAL OF CRAIOVA OVER A PERIOD OF 3 YEARS. THE USED MATERIAL IS REPRESENTED BY THE CLINICAL OBSERVATION SHEETS, SURGICAL PROTOCOLS AND THE DISCHARGE SUMMARIES OF THE PATIENTS. FOR THE PATIENTS INCLUDED IN THE STUDY A WIDE RANGE OF DATA WAS ANALYZED: AGE, SEX, ORIGIN, TYPES OF SURGERIES, INTRASURGERY ACCIDENTS AND INCIDENTS. THE RESULTS WERE IN ACCORDANCE WITH SPECIALTY LITERATURE AND THE CONCLUSIONS WE REACHED ON CERTAIN ASPECTS WERE" SLIGHTLY DIFFERENT" COMPARISON WITH THE ONES FROM THE SPECIALTY LITERATURE.

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KEYWORDS: ACUTE CHOLECYSTITIS, CHRONIC CHOLECYSTITIS, LAPAROSCOPIC CHOLECYSTECTOMY, INTRASURGERY ACCIDENTS AND INCIDENTS.

INTRODUCTION

Cholecystitis, an inflammatory affection which occurs in most cases as a complication of the vesicular lithiasis, appears in two forms: acute and chronic. The surgical approach of this pathology evolved significantly across the centuries, from the classical surgery which was practiced in the XIXth and XXth centuries, to the laparoscopic cholecystectomy introduced in 1987, which became the “golden standard” of surgeries nowadays.

The gallbladder pathology is dominated by vesicular lithiasis, this one affecting mainly feminine gender after 40 years old, stating that approximately 20% of the grown-up population suffers from this affection.⁸

Acute cholecystitis is characterized by the acute inflammation of the gallbladder wall, triggered in most of the cases by cholelithiasis. However, there are acute inflammatory conditions of the gallbladder which are alithiasic, more frequently met in men and associated with various etiologies: congenital defects of the bile ducts, secondary forms of sepsis conditions, parasitosis, post surgery or posttraumatic.⁹

Chronic cholecystitis is the most frequent disease of the gallbladder, 90% of the surgeries being made to treat this disease.

MAIN TEXT

I. THE AIM OF THE STUDY

The aim of the study is to make a retrospective analysis of the surgical treatment applied to the patients hospitalised for acute and chronic cholecystitis in The Surgery Clinic of the Railway Clinical Hospital of Craiova over a period of 3 years.

II. MATERIAL AND METHOD

The study was made in The Surgery Clinic of the Railway Clinical Hospital of Craiova on 332 patients diagnosed with acute and chronic diseases of the gallbladder over a period of 3 years, between 1st January 2014 and 31st December 2016, on whom a surgical curative treatment was applied by both classical and laparoscopic cholecystectomy.

The used material was represented by the clinical observation sheets, the surgical protocols and the discharge summaries of the patients. For each of the patients included in the study, the following data were analyzed:

- Age
- Sexul
- Origin and background
- The surgery type
- Intrasurgery incidents and accidents, the way these problems were solved
- Patient’s condition at the moment of hospital admission
- Patient’s condition at the moment of hospital discharge

⁸Papilian V, Albu I., 2001, Human Anatomy, Vol. 2: Splanhnology, Bucharest, BIC ALL, 127-148

⁹Mills S., 2004, Stenberg’s diagnostic surgical pathology, Philadelphia, Lippincott Williams and Wilkins, 1781-1783

The used study method was the clinical-statistical one, which consisted of making appreciations, comparisons and deductions on the obtained data. The data processing was made by means of Windows Microsoft Office 2007 and Windows Microsoft Excel 2007, the data was put down in charts, variability being represented in charts.

III. RESULTS

A. Repartition of the patients on age groups

The patients who were hospitalized and underwent surgeries at The Surgery Clinic for acute and chronic cholecystitis were between 14 and 85 years, the classification on age groups being noticed in *Figure 1*. Regarding the age distribution, we can notice a maximum of occurrence between the ages 51-70, representing 182 cases (54,81%), while under 41 years old, these diseases being less frequent, only 36 cases.

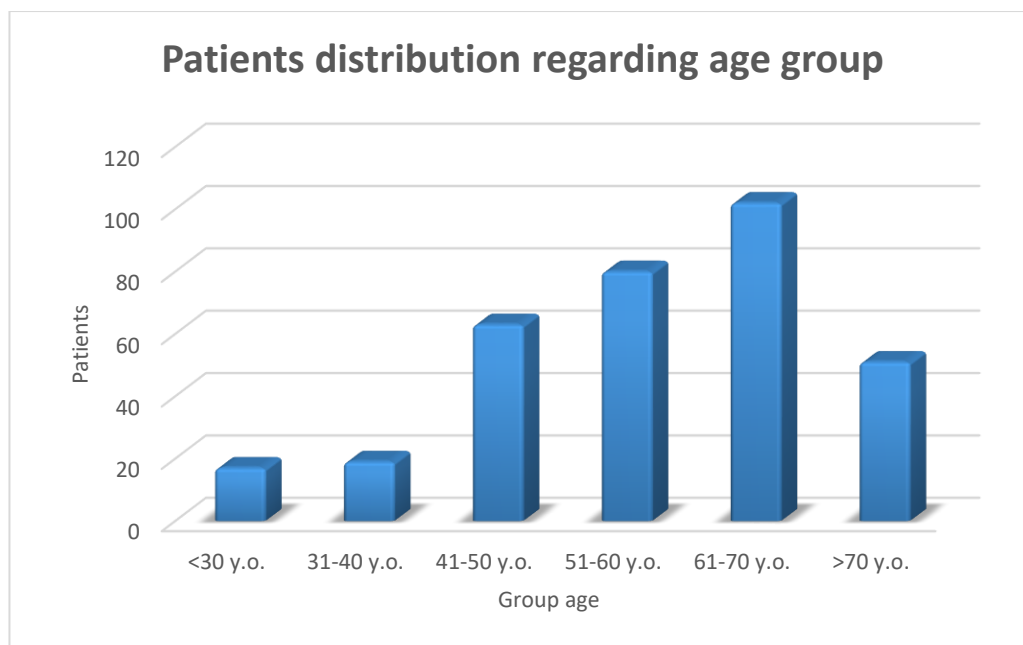


Figure 1. Age of patients included in the study

B. Patients ditribution according to gender

From the point of view of the repartition of patients according to sex, our study included 246 women (74,09%) and 86 men (25,91%), this also being in accordance with speciality literature which states a higher occurrence of this disease in women.

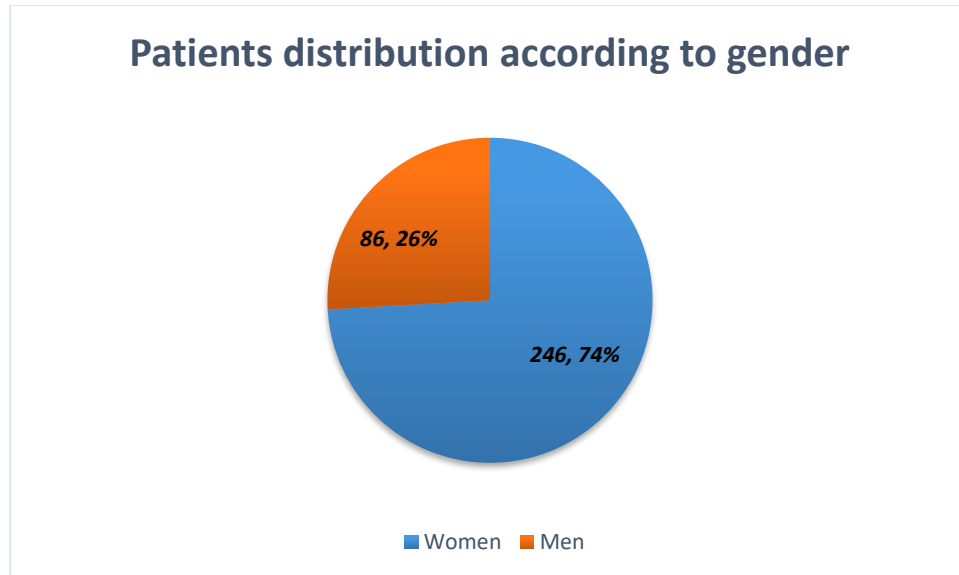


Figure.2. Distribution of the patients according to gender

Introducing the data about sex and age of the patients who underwent a cholecystectomy, we obtained the following Table:

Age	Women	Men	Total
Under 30 years old	15	2	17
31-40 years old	17	2	19
41-50 years old	50	13	63
51-60 years old	63	17	80
61-70 years old	72	30	102
Over 70 years old	29	22	51
Total	246	86	322

Table 1. Repartition of patients according to sex and age

From *Table 1* we can observe that if under 30 years old, the percentage of women of the total number of cases in that group age is overwhelming (88,2%), the older the patients are, the smaller the difference gets. Thus, between 41-50 years old, 79% of the patients are women and 21% are men, between 61-70 years old women represent 70,5% and men 29,5% of casses, while in the case of over 70 years old, in the same time with the existence of half number of surgeries, the report according to sex of the patients who underwent a cholecystectomy is 56,8% women and 43,2% men.

C. Patients distribution according to residence area

Regarding patients distribution according to residence area, we noticed a higher number of acute cholecystitis but also of chronic cholecystitis in the case of patients living in urban areas.

Thus, of the total of 332 cases, 255 (76,80%) patients were from urban area, while the rest of 77 patients were from rural areas representing 23,2% of the total number of cases.

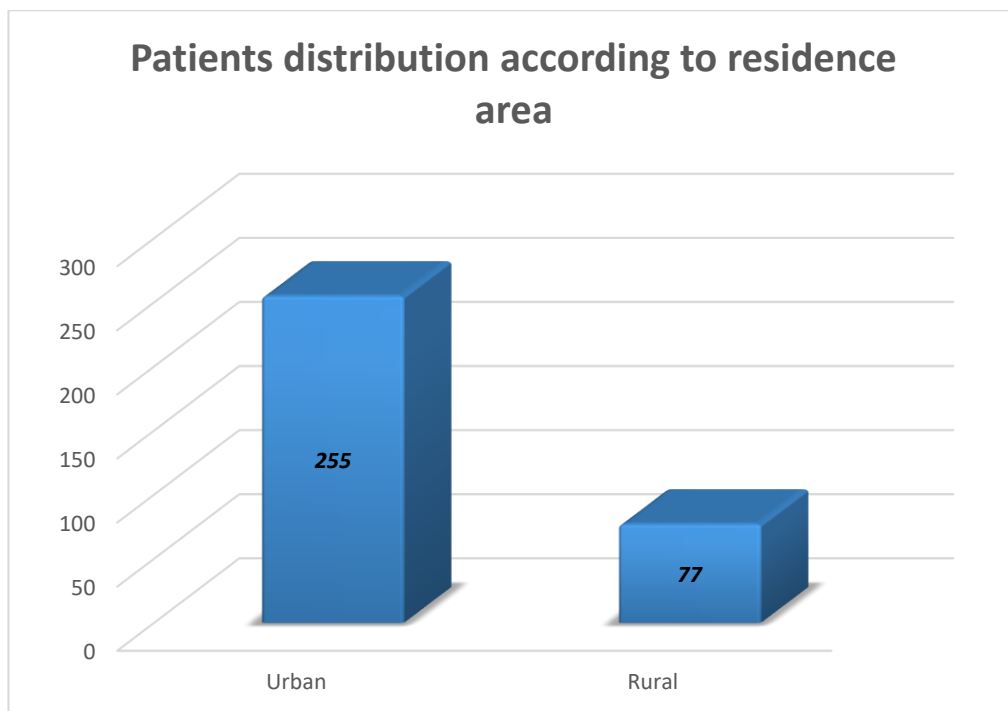


Figure 3. Patients distribution according to residence area

D. Surgery type

The acute or chronic inflamatory pathology of the gallbladder can be treated surgically using laparoscopic or classic techniques.

Surgery type	Acute cholecystitis	Chronic cholecystitis
1. Laparoscopic		
Retrograde	66	242
Anterograde	3	2
Bipolar	1	-
2. Classic	11	7

Table 2. Surgery types applied

Analyzing *Table no.2.* we can notice that in the case of chronic cholecystitis, the percent of patients who underwent laparoscopic surgeries is extremely high (97,2%), in comparison with 7 (2,78%) patients who underwent classical approach (*Figure 4*).

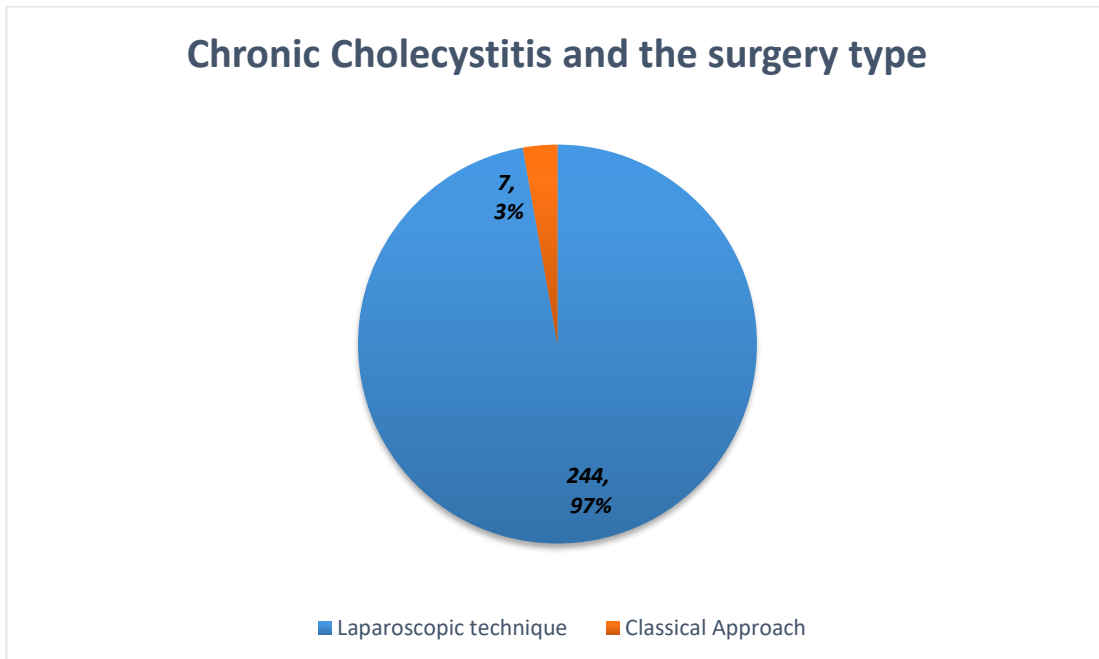


Figure 4. Chronic cholecystitis and the surgery type

Regarding acute cholecystitis, 70 patients (86,41% of the patients in this category) were performed laparoscopic approach , while 11 patients (13,58%) underwent classical surgery techniques (*Figure 5*).

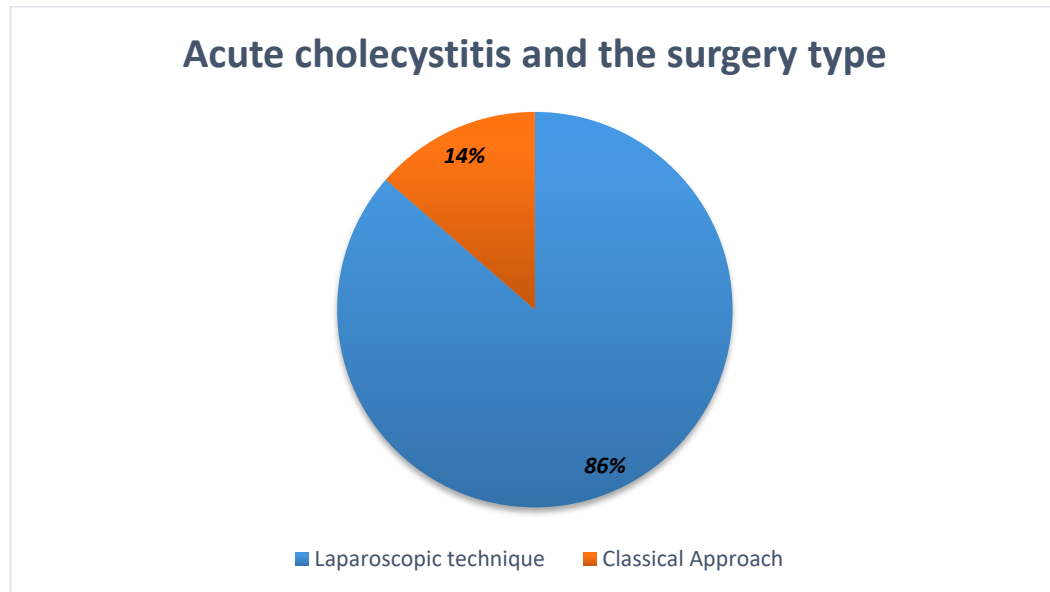


Figure 5. Acute cholecystitis and the surgery type

In what concerns the classic cholecystectomies, these were practiced more in the acute cases which presented more complications or choledocholithiasis of the main bile ducts, for the latter practicing more types of anastomosis: choledoco-duodenal witch latero-lateral anastomosis or termino-terminal choledoco-choledochal anastomosis.

IV. DISCUSSIONS

The surgical treatment of acute and chronic cholecystitis was individualized according to each patient's needs, taking into consideration the clinical form of the disease, the general condition of the patient, the comorbidities and paraclinical aspects in order to establish the therapeutic indications.

Pain is the main symptom in the pathology of the gallbladder, being described most frequently at the level of the epigastrium and the right quadrant, this thing being met at the patients included in our clinical study, the one at the level of the right quadrant being reported in all the cases, while the epigastric pains were met in approximatively one third of the cases.

The clinical manifestations which accompany the pain are the ones of the biliary dyspeptic syndrome: nausea, vomiting, postprandial bloating, heartburn, bitter taste, headache, regurgitation and lack of appetite, all of them being more frequently met throughout the evolution of the chronic cholecystitis than in the case of the acute pathology. In contrast, fever and rigors, clinic signs of an infection, were more frequently met in acute cholecystitis. The mechanic jaundice met in 3 cases was associated with the rest of the characteristic elements of post-hepatic jaundice: dark urine and acholic feces.

In what concerns the objective examination of the operated patients, 40% had the mass index over 30, underlining the importance obesity has in the pathogenesis of cholelithiasis, which is the main cause of inflammatory conditions of the gallbladder. Moreover, the Murphy sign—represented by deep pain felt by the patient when breathing profoundly during the examination of the cystic spot, occurred at 30% of the patients suffering from chronic cholecystitis and 61% of the patients suffering from acute cholecystitis.

Abdominal ultrasound represented an investigation with a major role in the orientation of the diagnosis and surgical indication, the existence of gallstones with rear shadow cone establishing the lithiasis etiology of the acute or chronic disease. Thus, only in the situation of 10 cases the lithiasic origin of the gallbladder pathology could not be highlighted, these representing only 3% of the analyzed cases.

Regarding echographic aspects which are useful for the orientation of the positive diagnosis of cholecystitis, acute cholecystitis was more frequently correlated with certain ultrasonographic aspects such as: biliary sludge in a variable quantity, the hypoechogenic walls of the gallbladder which show the parietal edema, the increased size of the cholecist, zones of parietal necrosis, the double outline of the wall or the intravesical polyps. The echographic aspects which highlighted a chronic gallbladder pathology were the hyperechogenic, thicker walls of the gallbladder but also the scleroatrophic aspect, sometimes with a gallbladder molded on calculus.

The ultrasonographic signs of a potentially difficult surgery are: a thicker wall of the gallbladder, contracted gallbladder, the whole cavity of the gallbladder is filled with gallstones, calcified gallbladder, pericholecystic liquid and air in the wall of the gallbladder (emphysematous cholecystitis), acute gangrenous cholecystitis, sessile gallbladder.¹⁰

In the case of chronic cholecystitis patients, the indication of the surgical treatment is compulsory when it is diagnosed, except the counterindications due to the risk factors (severe cardiac affections, decompensated organ failure). However, the treatment can be individualized according to the symptomatology of the patient and the risk of complications. Thus, for patients with extremely reduced symptomatology, the risk of complications is between 1-3%/year, being possible to accept adopting a corresponding hygienic-dietary regime and periodical reevaluation from the clinical and paraclinical point of view. In exchange, for patients with recurrent or severe symptoms there is a percent of complications of 7%/year, so cholecystectomy is to be discussed here. The surgical indication is clear mainly in the cases of:

- Chronic microscopic cholecystitis with micro-gallstones under 3 mm (danger of migration and complications such as angiocholitis or cholangitis acute pancreatitis), situation met in 5 cases;
- Scleroatrophic chronic cholecystitis (risk of complications such as internal fistulas), met in 11 cases;
- Chronic cholecystitis with successive cramps, cholelithiasis in patients under 50 years old (risk of degeneration);
- Complications (acute cholecystitis, jaundice, angiocholitis, acute pancreatitis, bilio-biliary or bilio-digestive fistulas).

¹⁰Arshad M. M., 2011, *Advances in Laparoscopic Surgery*, Croatia, InTech, 13-28.

In Romania radical intervention is preferred both in the case of silent forms of affected gallbladder, thus making a prophylaxy of septic, mechanical or degenerative neoplastic complications.¹¹

Acute cholecystitis is a surgical emergency, its treatment imposing an emergency cholecystectomy. Despite this fact, the anatomio-clinical polymorphism of the acute cholecystitis leads to a difficulty in establishing the therapeutic strategy theoretically and practically. The surgical moment is chosen according to the anatomical and clinical form:

- Immediate emergency: over acute forms, regardless the risks. These cases are represented by the acute cholecystitis with peritonitis, respectively the gangrenous forms with fast aggravation;
- Postponed emergency 24-72 hours: attitude which is adopted in most of the cases of acute cholecystitis;
- Surgery after timing (3-7 up to 10 days) in the case in which other comorbidities must be investigated;
- Surgery after the cooling of the process, in the case in which the patient refused the former surgery or the medical conservative treatment was chosen.¹²

Taking into consideration the prophile of our surgical section chirurgicale, most of the surgeries were postponed emergencies, except three cases of acute cold cholecystitis lithiasis and a case of acute cold pio-cholecistitis lithiasis.

The prophylactic antimicrobial therapy supposes the administration of a broad-spectrum antibiotic such as one administration of cefalosporines which precedes the surgery with a few hours, treatment applied in the case of all patients. The antimicrobian curative treatment is applied post-surgery in the case of complications or local infections at the level or at a distance of the wound.

In what concerns the surgery type made, 94,57% of the total number of cholecystectomy interventions were laparoscopic, confirming the status of the present “golden standard” of surgeries at the level of the gallbladder, being the most practiced major abdominal surgery in modern countries.

This minimally invasive intervention presents a series of advantages which establish its indication, such as the important decrease number of days in hospital with a faster social reinsertion, the higher comfort of the patient through reducing pain and post surgery ileus, less frequently met suppuration and eventration in comparison with the classical technique, esthetic advantage due to the fact that incisions are much smaller.

However, despite the numerous advantages proved in various clinical studies, laparoscopic cholecystectomy presents a series of disadvantages which had to be taken into consideration in the moment of establishing the thearapeutic decision. Thus, the absolute contraindication of this type of surgery are the impossibility of tolerating the general anesteheisia, refractory coagulopathy and gallbladder cancer. In the case of the intra-surgery diagnosis of this affection, the conversion into an open surgery is compulsory, for a higher control of rezection limits and for the lymph nodes extrirpation.

¹¹Angelescu N., 2003, Surgical pathology Treaty , Bucharet, Medical Ed., 421-460, 1899-1983.

¹²Ghelase F., Georgescu I., 1999, General Surgery, Didactic and pedagogical publishing house, Bucharest 338-369.

Numerous situations which were previously considered as contraindications of the laparoscopic approach (gangrenous cholecystitis, gallbladder empiem, biliary enteric fistula, obesity, pregnancy, the ventriculoperitoneal shunt, cirrhosis, pathological personal history of surgeries at the level of the superior abdominal part) are no longer considered contraindicated, but cases which require a special pre- operatory preparation and a thorough rigorous cost-benefit assessment..

Classical cholecystectomy is the surgery which was done in a number of 11 cases of acute cholecystitis and 7 cases of chronic cholecystitis.

In the case of acute cholecystectomies, the pathologies which imposed a classical cholecystectomy were choledohcal lithiasis and migrated choledochal lithiasis, these being solved through a choledocholithotomy and a latero-lateral choledochoduodenostomy. The existence of abscesses at the level of the peritoneal cavity, such as the pericholecystic or and the interhepato-diaphragmatic abscesses were treated through peritoneal lavage and drainage.

In the case of a patient who presented the secondary diagnosis of choledochal calculus, hepatic pediculitis and perivisceritis, a biliary external drainage was compulsory through a Kehr tube, the choledocholithotomy and the viscerolysis. Choledochotomy and the latero- lateral anastomosis between the bile duct and the duodenum were compulsory in a case with cholecystoduodenal fistula and in another case with choledochal calculus, chronic oddity under observation and mechanical jaundice.

During the surgeries there were some intra-surgery accidents and incidents which could not be solved through laparoscopic surgery, converting the surgery into a classical one, some of which are going to be presented in detail.

In the case of a 50year-old patient, with the diagnosis of chronic lithiasic cholecystitis which underwent a retrograde laparoscopic cholecystectomy, a punctiform lesion of the main bile duct was made with a Hook clip during the surgery, this incident being acknowledged intra-surgery. In this situation two therapeutical procedures can be applied: converting the laparoscopic surgery into a classical one with a Kehr tube, respectively making a multiple drainage around the lesion of the main bile duct, continuing the surgery laparoscopically. The second choice was adopted. After that, on the first three days after the surgery there was a leak of gall of 300-400 ml/day, which decreased on the fourth day, and stopped on the fifth day. The patient was discharged from hospital on the eighth day after the surgery in good general condition.

A second case is that of a patient of 48 years old hospitalized for acute lithiasic cholecystitis who had an intra-surgery incident when, at the moment of introducing the trocar at the level of the umbilical scar, a wound was produced at the level of the right common iliac vein thus a massive haemoperitoneum occurred which was not recognised immediately, leading to a drop of blood pressure and a raise of heartbeats up to 130 beats/minute. In this context, the patient was immediately resuscitated, and the laparoscopic surgery was rapidly converted into a classical one, finding a wound of approximately 3-4 mm at the level of the la nivelul right common iliac vein which was stit with great difficulty, thus stopping the bleeding. The patient received massive blood transfusions, the evolution was favourable and she was discharged on the tenth day after the surgery.

A case of conversion of laparoscopic approach into a classical one was of a 76 year old man, with the diagnosis of acute lithiasis pio-cholecystitis, who was hospitalized for pains in the epigastrium and in the right quadrant, postprandial bloating, morning bitter taste, heartburt, nausea

and selective lack of appetite. During the surgery an intense process of perivisceral inflammation under the liver made it impossible to visualize the gallbladder after the viscerolysis manoeuvres. The conversion of the surgery is decided upon; after the adhesiolysis, we can notice the existence of a process of hepatic pediculosis, and the gallbladder presented a thick wall. The infundibulo-cystic area is dissected with difficulty, and in that moment a lesion of the main bile duct is produced. A cholecystectomy was made and the damaged bile duct was restored through termino-terminal choledoco-choledochal anastomosis protected with a T tube (Kehr). The post-surgery evolution was favourable.

Another case is that of a woman with chronic scleroatrophic cholecystitis in which the ultrasound highlighted a gallbladder molded on the gallstones. Thus, a laparoscopic cholecystectomy was attempted, but during the surgery, the intervention could not be done because of the intense perivisceritis and pediculosis at this level. Later, the atrophy degree of the gallbladder which made a radical classical surgery impossible, thus, an incomplete cholecystectomy was performed, remaining a gallbladder end which contained a big dimensions gallstone (about 1.5 cm). The persistence of the biliary suffering expressed subjectively under the form of an intense dyspeptic syndrome which persisted after the surgery imposed a new surgery after about 2 months with a total cholecystectomy which was made without any incidents.

The fifth case is that of a patient which was hospitalized with the diagnosis of chronic cholecystitis who underwent laparoscopic cholecystectomy without intra-surgery incidents. Despite this fact, during the doctor's visit she showed signs of sweating, she was sleepy, and colourless, she had tachycardia (120 beats/ minute) and low blood pressure (50/30 mmHg), but on the drainage tube there was no blood leaking. An emergency surgery was decided upon, performing a midline xifo-umbilical laparotomy evacuating blood clots and quantities of blood of approximately 1.5 liters, the cause of this bleeding being the skidding of the clip from the level of the cystic artery. Thus, a ligature was made at the end of the cystic artery also with the draining of the subhepatic space. The evolution was good and the patient was discharged from hospital one week after the surgery.

The sixth case was represented by a young 28 years old patient who underwent laparoscopic cholecystectomy. He suffered a lesion of the hepatic duct which was not recognised during the intervention. After the surgery, about 1.5 liters a day of gall which persisted for 10-12 days was drained. Thus, in order to set a precise diagnosis, a cholangiography was done, observing the partial section of the right hepatic duct. The patient was transferred a fost transferat to another Surgery Clinic, where he underwent an endoscopy.

V. CONCLUSIONS

- In the study groups, the chronic cholecystitis was much more frequent than acute cholecystitis.
- The division on sexes showed that biliary diseases were more frequent in the case of women than in the case of men.
- The inflammatory diseases of the gallbladder were more frequent in the case of the patients of 51-70 years old living in urban areas.
- The abdominal ultrasound was the main paraclinical investigation used in the diagnosis of cholecystitis, in the majority of cases revealing the presence of gallstones.

- The laparoscopic cholecystectomy became the gold standard of the treatment of biliary pathology in the last two decades, 94,57% of the surgeries made during the clinical study being made through laparoscopic technique.
- The advantage of the laparoscopic cholecystectomy is clearly superior to classic cholecystectomy, the patients being faster inserted into society, the pain and the hospitalization after the surgery being lower, immediate or further complications being almost inexistent.
- The conversion of the surgery from laparoscopic into classical one is a proof of surgical progress not a failure, this being imposed by the extensive inflammatory processes, important fibrosis or iatrogenic lesions of the main bile ducts.
- The multidisciplinary approach and solving the case in due time in order to repair the biliary lesions are essential for obtain best results.
- Although specialty literature states that the number of hospitalization days is low, only a few days, in the case of laparoscopic surgeries, our study showed the fact that most of the cases were included in the group of patients who were hospitalized for a period of 5-10 days.

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CONSERVATIVE SURGERY - THE ALTERNATIVE WITH GOOD RESULTS IN MAMMARY CANCER

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ABSTRACT

THE MAMMARY NEOPLASM IS THE MOST FREQUENTLY MET ANOMALY FOR THE FEMININE GENDER CONSTANTLY BEING A TOPICAL ISSUE IN THE FIELDS OF ONCOLOGY AND SURGERY.

IN ROMANIA THE PROBLEM OF BREAST CANCER CAN BE CONSIDERED A REAL ALERT , DUE TO THE FACT THAT MORE THAN 50 % OF THE WOMEN ARE DIAGNOSED WHEN THE STAGE OF THE DISEASE IS ADVANCED.

THE MAIN THERAPEUTICAL PROCEDURES ARE SURGERY, RADIOTHERAPY, CHEMOTHERAPY, HORMONE THERAPY, IMMUNOTHERAPY OR MOLECULAR THERAPY AND GENE THERAPY.

THE CLINICAL STUDY WAS MADE BY MEANS OF A RETROSPECTIVE ANALYSIS OF MAMMARY NEOPLASM CASES USING THE INFORMATION FROM OBSERVATION AND ONCOLOGICAL SHEETS OF THE PATIENTS WHO UNDERWENT SURGERIES. THE DOUBLE PURPOSE OF CONSERVATIVE SURGERY IS TO GET A GOOD LOCAL CONTROL OVER THE DISEASE ON THE LONG TERM AND A MINIMUM LEVEL OF LOCAL MORBIDITY .

THE POST SURGERY RESULTS AND THE CONCLUSIONS WE HAVE REACHED WERE ENCOURAGING BEING IN ACCORDANCE WITH SPECIALISED LITERATURE.

KEY WORDS: CONSERVATIVE SURGERY, MAMMARY CANCER, CHEMO-RADIOTHERAPY.

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I. INTRODUCTION

Breast cancer is the most frequently met anomaly for the feminine gender⁸, constantly being a topical issue in the fields of oncology and surgery. This fact is due to the frequency of this disease which continues to persist at high values, and its evolution is severe especially when it is diagnosed in a late stage of the disease⁹. Over time, however, new ways have emerged to reduce breast cancer mortality. Thus, breast screening that allows the discovery of the disease in less advanced stages or prior to clinical manifestations, where the number of healings increases considerably.¹⁰

In Romania the breast cancer issue can be considered a real alert when referring to the fact that more than 50% of the women with mammary cancer are diagnosed when the disease is in an advanced stage and that is why the therapy costs a lot more and the results are less satisfying.¹¹ This warning sign must lead to a prevention and early detection programme for the neoplasm of the mammary gland.¹²

THE MAMMARY CANCER TREATMENT

The surgical oncology treatment of the breast is complex and adjusted to each case according to: age, patient's characteristics, the clinical and histological stage of cancer, the evolution stage of the disease,¹³ the hormone status and the evolution rhythm of the tumor.¹⁴

Before the treatment, a balance is established which can offer information about the real extension of the disease (the TNM stage), the agresivity of the tumor (how fast it evolved in the last 2-3 months)¹⁵ and the condition of the vital organs.¹⁶ The minimal investigations are compulsory to allow the observation of the vital organs are: CBC (Complete Blood Count), glycaemia, hepatitis tests, renal function tests, coagulation tests, tumoral markers like CA 15-

⁸Kelsey J.L. – Breast cancer epidemiology: summary and future directions. *Epidemiol Rev*, 1993, 15(1):256-63.

⁹Şuteu O., Ghilezan N., Todor N., Scorţan E. – Epidemiologia cancerului mamar în România. În: Gh. Peltecu, *Tratamentul conservator al cancerului mamar incipient*. Editura Universitară „Carol Davila”, Bucureşti 2003, pag.9.

¹⁰Prişcu Al. – Patologia glandei mamare. În: *Prişcu Al. (sub red.) Chirurgie*, vol. I. Editura Didactică şi Pedagogică R.A., Bucureşti, 1995, 479-528.

¹¹Peltecu G., Ionescu M., Lesaru M., Anghel R., Minea N., Laura O, Median D. – Cancerul de sân. În: *Irinel Popescu (sub red.)* *Tratat de Chirurgie*, vol. VIII. Editura Academiei Române, Bucureşti, 2008, 779-802.

¹²Bland K., Vezeridis M. – Sânul. În: *Schwartz S., Shires T., Spencer F. (sub red.)* „Principiile chirurgiei”, vol. I. Editura Teora, Bucureşti, 2005, 544-610.

¹³Bălănescu I., Blidaru Al. – Cancerul sânelui. În: *Angelescu N. (sub red.)* „Tratat de patologie chirurgicală”. Editura Medicală, Bucureşti, 2001, 1187-1206

¹⁴Angelescu N., Jitea N., Cristian D. – Actualităţi în diagnosticul şi tratamentul cancerului mamar. În: Dragomirescu C., Popescu I. (sub red.) „Actualităţi în Chirurgie”, Ed. Celsius, Bucureşti, 1998, 48-586. Olsen O., Gotzsche PC. – Screening for breast cancer with mamography (Cochrane review), *Cochrane Database Syst Rev* 2001:4.

¹⁵Bland K., Vezeridis M. – Sânul. În: *Schwartz S., Shires T., Spencer F. (sub red.)* „Principiile chirurgiei”, vol. I. Editura Teora, Bucureşti, 2005, 544-610.

¹⁶Greenal M.J. – Cancer of the breast. In „Oxford Textbook of Surgery on CD-ROM”. Oxford University Press – AND Electronic Publishing B.V., 1995, 808-838.

3, EKG and imagistic studies: pulmonary Rx, liver ultrasonography, skeleton Rx, bone scintigraphy and CT-computed tomography (thorax, skull, abdomen) if needed.¹⁷

The main treatment ways are surgery and radiotherapy (which allow local control over the disease), chemotherapy, hormone therapy, immunotherapy or molecular therapy and genetic therapy (which allow sistemic control over the disease).

CONSERVATIVE SURGERY

After classical surgery, conservative treatment has become a remarkable way of progress¹⁸ in the issue of mammary cancer of limited dimensions.¹⁹ The greatest advantage of conservative techniques is that it modifies the breast the least²⁰ and thus it can be considered both an advantage for the patients mental state.²¹

The conservative therapy is recomended in certain selected cases: in malignant tumors stages I and II, with tumor dimensions smaller than 2 cm and in the case in which the patient wishes to keep her breast; relatively contraindicated in the case of : tumors with dimensions between 3-5 cm, multiple tumors in the same quadrant, deep tumor, enlarged axillary adenopathy , recurrences after conservative surgeries²², Ductal carcinoma in Situ and Lobular Carcinoma in Situ, history of collagen diseases (LES or scleroderma); and totally conterindicated: tumors with bigger than 5 cm dimensions, 2 tumors in different quadrans, pregnancy (irradiation is counterindicated), diffuse microcalcifications difuze on the mammography.²³

The conservative treatment reffers especially to the primary mammary tumor and axillary lymph nodes.

a. The surgery of the primary tumor is dictated by the tumor dimension compared to the size of the breast, a lot of conserving techniques have been described in this respect: wide local excision(sectorectomy, quadrantectomy).

Regardless the peritumoral excision, there is a high probability that neoplastic cells are still present. That is why, in order to diminish the recurrence risk, post surgery irradiation is absolutely necessary, which has the capacity to control the disease locally. Radiotherapy can start two weeks after the surgery or when the wound has healed. The results of conservative surgery post-irradiation indicate total survival and no recurrences for 90% of the cases. Lack of post-surgical irradiation increases the risk of loca recurrence 25-45%.²⁴

¹⁷Angelescu N., Popa E., Bordea A., Jitea N., Burcoş T., Florea I., Aldea C., Zodieru Ileana – Strategia terapeutică în cancerul mamar local avansat. Chirurgia, 2002, 97(4):357-363.

¹⁸Bland K., Vezeridis M. – Sânul. În: Schwartz S., Shires T., Spencer F. (sub red.) „Principiile chirurgiei”, vol. I. Editura Teora, Bucureşti, 2005, 544-610.

¹⁹Badulescu M.F. – Curs de oncologie clinică și nursing în oncologie. Editura medicală, Craiova, 2015, pag:35-73.

²⁰Mogoş D., Vasile I., Păun I. – Pledorie pentru chirurgia conservatoare a sânelui. Chirurgia, 1998, 93(4):239-628.

²¹Mogoş D., Vilcea D., Vasile Ionescu M., Păun I., Teodorescu M., Ţenovici Mihaela, Florescu M. – Chirurgia conservatoare a sânelui – 7 ani de experienţă, Chirurgia, 2003, 98(3):225-236.

²²Bălănescu I., Blidaru Al., Duşa Rodica – Criteriile și locul chirurgiei limitate în tratamentul cancerului mamar, Revista de Chirurgie, 1991.

²³Farrar W.B. LaValele G.J., Kim J.A. –Breast Cancer, Cancer Surgery, McKenna R.J., Murphy Lippincott Company Philadelphia, 1994.

²⁴Bălănescu I., Blidaru Al. – Cancerul sânelui. În: Angelescu N. (sub red) „Tratat de patologie chirurgicală”. Editura Medicală, Bucureşti, 2001, 1187-1206

Moreover, it is also very important that, intraoperative, the histopathological extemporaneous test should be done from the removed pieces/margins, in order to determine the positivity or negativity of the piece and establish the surgical procedures.²⁵

b. The surgery of axillary lymph nodes is part of the conservative surgical treatment as the mammary cancer metastases frequently in the axillary lymph nodes.

The surgery of the sentinel lymph node is a technique which revolutionizes the surgery of the axillary lymph nodes. The concept of the "sentinel lymph node" refers to the first axillary lymph node, which can be invaded by neoplastic cells through lymphatic drainage. The state of the sentinel lymph node reflects the situation of the whole axilla/ armpit.²⁶ If the sentinel lymph node is located and it proves to be non-invaded histopathologically, then a useless axillary dissection is avoided.²⁷

RADIOTHERAPY

It is an essential component in the treatment of mammary cancer, especially for the local or regional control of the disease, being recommended in the incipient stages of the disease when the conservative surgery is advisable or in the case of postmamectomies taking into consideration the dimensions of the tumor (>5 cm); the invasion of the regional lymph nodes, of the tegument and muscles and also the positive resection margin.

CHEMOTHERAPY

According to the moment (before or after the surgery) when it is applied, there is:

a. Adjuvant chemotherapy: is applied post surgery .

b. Neo-adjuvant chemotherapy: is applied preoperative, in advanced tumors for conversion to surgery state or in the case of smaller but more aggressive tumors;

It is advisable in IIA – IIIC stages.

c. Palliative Chemotherapy : is advisable especially in the case of patients with metastatic disease without hormone receptors and with distant metastases or who have hormonoresistance.²⁸

In the case of anthracycline resistance we can use Taxanes (paclitaxel, docetaxel), Vinorelbine, Gemcitabine.²⁹

HORMONE THERAPY

It is the essential key in the treatment of mammary cancer for the patients with positive estrogen and progesterone receptors (HR+). Tamoxifen reduces the recurrence risk up to 10

²⁵Tartter P.I., Kaplan J., Bleiweiss I. – Lumpectomy margins, reexcision and local recurrence of breast cancer, The American Journal of Surgery, 179; 81-85, 2000.

²⁶Bălănescu I., Blidaru Al. – Cancerul sâului. În: *Angelescu N. (sub red) „Tratat de patologie chirurgicală”*. Editura Medicală, București, 2001, 1187-1206

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years and aromatase inhibitors (Anastrozole, Letrozole, Exemestane) are better tolerated, without any adverse effects and without inducing any resistance. Also, Gn-RH agonists (Zoladex) can be used - which attempts a medical castration, which has, however transitory effects.³⁰

MOLECULAR TARGET THERAPY

The election indications of target therapy aims at metastatic mammary cancer types which are also resistant to chemo-hormone therapy. Recently, the Trastuzumab is advisable for HER2/neu positive patients with the presence or absence of lymph nodes invasion, but with tumoral dimensions bigger than 1 cm.³¹

For HER2/neu negative patients Bevacizumab is advisable, which is an anti-angiogenic therapeutic agent, more precisely anti-VGEF.³²

II. THE IMPORTANCE AND OBJECTIVES OF THE STUDY

About 25 years ago, the treatment of mammary cancer types, even of reduced dimensions, still stipulated radical techniques of approaching the breast, such as: radical Halsted mastectomy, radical or modified Patey mastectomy, which had a mutilating character and major aesthetic-cosmetic consequences, and most times young patients remained with a psychological trauma. Today, due to knowledge extinction in the domain of mammary cancer biology, association of radiotherapy, chemotherapy and molecular target therapy became possible that the surgical act to be limited, without affecting survival at 5 and 10 years.

Of the total 142 cases with breast cancer, operated in the clinic, only 53 cases benefited from conservative surgical treatment. From the 1st of January 2014 until the 31st of December 2017, depending on the distribution according to years there were:

- in 2014 – 9cases;
- in 2015 – 15cases;
- in 2016 – 12 cases;
- in 2017 – 17cases;

The major advantages of the surgical conservative treatment are:

- they offer acceptable cosmetic results;
- psychological morbidity is much lower;
- major effects like (anxiety, depressive episodes) are reduced;
- they give trust to the patient;
- sexual life is less affected.

³⁰Peltecu G., Ionescu M., Lesaru M., Anghel R., Minea N., Laura O, Median D. – Cancerul de sân. În: *Irinel Popescu (sub red.)* Tratat de Chirurgie, vol. VIII. Editura Academiei Române, București, 2008, 779-802

³¹Peltecu G., Ionescu M., Lesaru M., Anghel R., Minea N., Laura O, Median D. – Cancerul de sân. În: *Irinel Popescu (sub red.)* Tratat de Chirurgie, vol. VIII. Editura Academiei Române, București, 2008, 779-802

³²National Comprehensive Cancer Network – Clinical Practice Guidelines in Oncology – v 2007 – Breast Cancer – <http://www.nccn.org>.

III. MATERIAL AND METHOD

This clinical study was done using a retrospective analysis of the neoplasm mammary cases, using informations from patient's observation and oncological sheets who have underwent a conservative surgery on the breast. The patients were diagnosed and treated in The Surgery Clinic of the Railway Clinical Hospital of Craiova, over a period of 4 years (1st of January 2014 – 31st of December 2017).

The conservative surgery of the breast was made following the surgery protocol of Milan, which supposes practicing this type of surgery for the mammary tumors in stages I or II (T1N0-1M0 or T2(<3cm)N0M0 (sectorectomy + axillary lymph nodes removal + radiotherapy on the breast; if post surgery N is positive (N+), chemotherapy and hormone therapy are applied, but if N is negative (N-) hospital care and periodical controle is necessary).

Over the last 4 years (2014-2017) thanks to the good results obtained through conservative surgery (absence of local recurrences) the field of conservative surgeries has been enlarged for the tumors of more than 3 cm up to 5 cm.

IV. RESULTS

As we have already mentioned, the number of mammary neoplasm diagnosed cases in stages I and II in The Surgery Clinic of the Railway Clinical Hospital of Craiova registered a sudden growth between 2014 and 2015, decreasing in 2016, slightly increasing again in 2017 (Table 1).

YEAR	NUMBER OF CASES
2014	9
2015	15
2016	12
2017	17
TOTAL	53

Table no. 1 – The distribution according to years of the mammary neoplasm cases which underwent conservative surgeries

From the **etiopathogenic** point of view it was difficult to establish which risk factors were involved and up to what proportion they dominated the pathology of breast, however, the genetic factor (the family genetic inheritance) was present in 15 of the 53 cases. In 6 of the 15 cases, the patients had first degree relatives diagnosed with mammary cancer (mother and one sister), and in the other 9 cases the patients had second and third degree relatives diagnosed with mammary neoplasm.

Sex	Men	Women
<i>Number of cases</i>	1	52
<i>%</i>	1,88	98,11
Residence area	Urban	Rural
<i>Number of cases</i>	31	22
<i>%</i>	58,49	41,50

Table no.2 – Patients distribution according to sex and origin

From Table no. 2 we can notice a prevalence of the patients in the urban areas (31cases) in contrast with the rural areas (22 cases). The larger number of patients from the urban area can be due to the addressability of a large number of patients in The Surgery Clinic of the Railway Clinical Hospital of Craiova or due to the age group (51-60 years old) with a higher frequency of cases in the urban area. (*Figure 1*).

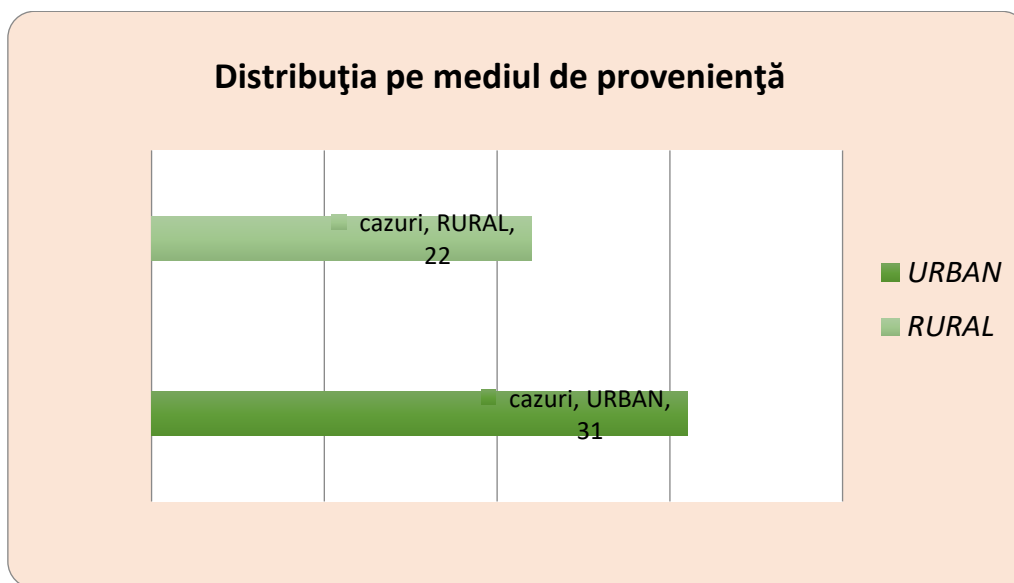


Figure 1. Patients distribution according to residence area

- Among **the risk factors** encountered in the group of patients there can be mentioned:
- *obesity* – 13 cases (24,8%), but without making a distinction between the premenopausal or postmenopausal obesity;

- *hormone imbalance;*
- *administration of oral hormone products* (estrogen or mixed) – met in 7 cases, used for the treatment of certain problems in the genital sphere and not as a contraception method;
- *small and repeated traumas* – were met in only one case, as an effect of long lasting professional activities (35 years of work at the sewing machine);
- *exposure to röntgen radiations* –3 persons had a history of more than 3 X-rays a year;
- *breast exposure to UV radiations* – 2 cases;
- *endocrinological disorders;*
- *stress* – 11 cases, in which the following stress factors were present (deaths of family members, long-lasting conflicts) (Figure 2)

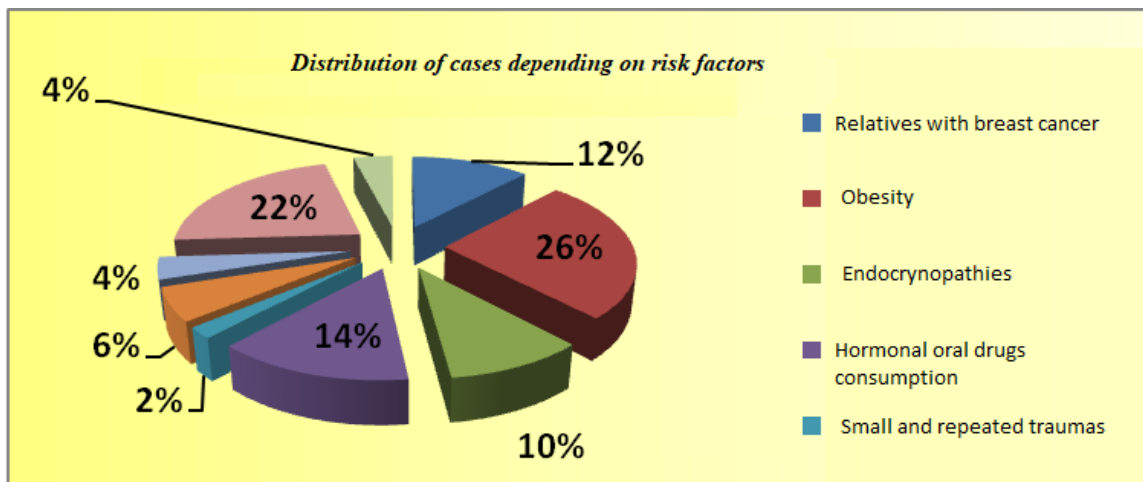


Figure 2 – Distribution of cases depending on risk factors

The average age of the patients with mammary neoplasm was 50 years old clasified on group ages between 25 to 89 years old. (Figure 3)

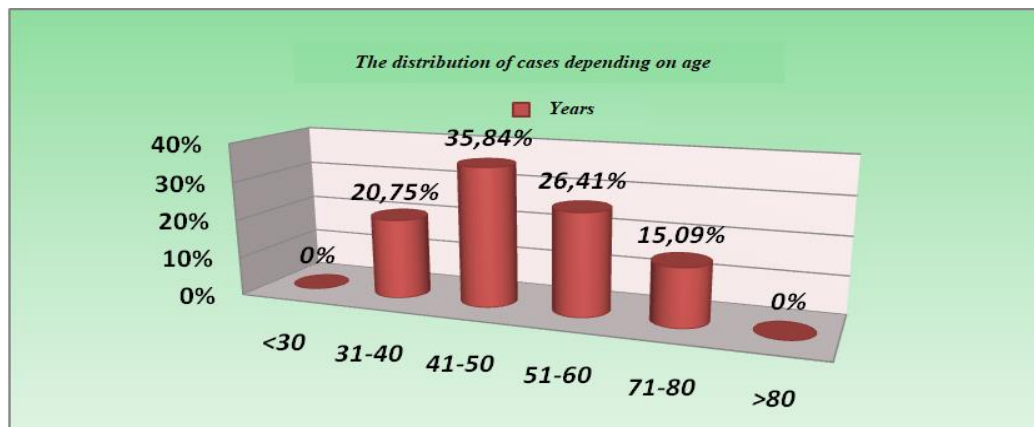


Figure 3 –The distribution of cases depending on age

According to personal medical history, we noticed that in 9 cases of the 53 studied cases there were presented significant personal medical history facts (Figure 4):

- 3 cases with bilateral carcinoma;
- 1 cases with contralateral mammary neoplasm;
- 2 cases with ipsilateral neoplasm ;
- 2 cases of ipsilateral mastitis;
- 1 cases with fibrocystic ipsilateral mastose;

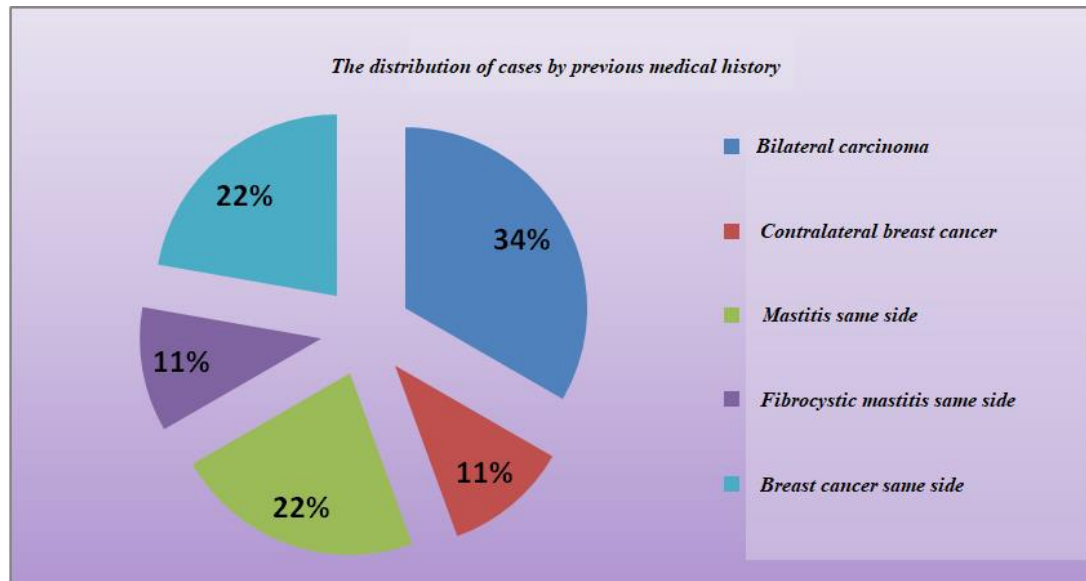


Figure 4 – The distribution pf cases by previous medical history

The macroscopic aspect of the tumor

From the macroscopic point of view all the tumors were solid, with an infiltrative aspect, of thick consistence, white- grey with yellowish zones, also, there were necrosis areas, bleeding, calcifications on a few pieces; most of the formations were unique.

The microscopical analysis of the tumor (the histologic types of tumors)

- *ductal carcinoma:*
 - ductal „in situ” (DCIS) – in 4 cases;
 - invasive ductal (DIC) – in 29 cases;
- *lobular carcinoma:*
 - lobular „in situ” (LCIS) – in 3 cases;
 - lobular invasive (LCI) – in 11 cases;
- *mixed ducto-lobular carcinoma (MDL-C):* 3 cases;
- *Paget Disease:* 1 case
- *Mucinous carcinoma:* 2 cases; (Table no. 3)

HISTOPATHOLOGICAL TYPE	NO. OF CASES (%)
„in situ” tumors:	7 (15,09)
Intraductal solid carcinoma	2 (3,77)
Intraductal cribriform carcinoma	1 (1,88)
Intraductal comed type carcinoma	1 (1,88)
Intralobular carcinoma	3 (5,66)
Paget Disease	1 (1,88)
Invazive carcinoma:	45 (84,90)
Ductal invasive carcinoma	29 (54,71)
Lobular invasive carcinoma	11 (20,75)
Mixed Ducto-lobular carcinoma	3 (5,66)
Mucinous carcinoma	2 (3,77)

Table no. 3 – Histopatological types

The analysis of cell differentiation / Nottingham grading (NG)

The BR degree is a useful and important parameter concerning the prognosis. In the study group we observed an important percentage of tumors with a high degree of differentiation, which is a bad prognosis. In the studied group we observed an important numbers of tumors with high differentiation degree, which is equivalent with a bad prognosis.

The mammary carcinomas which were analysed in system G through Nottingham grading (*Figure 5*):

- First degree (well differentiated) score 3-5: 4 cases;
- Second degree (moderately differentiated) score 6-7: 9 cases;
- Third Degree(weakly-diferentiated) score 8-9: 40 cases.

According to the difference degree of mammary carcinomas we noticed that most of the cases were :

- weakly diferentiated carcinomas – third degree (75,47%),
- the fewest were the well-diferentiated – first degree (7,54%),
- the second were the moderately -diferentiated ones – second degree2 (16,98%).

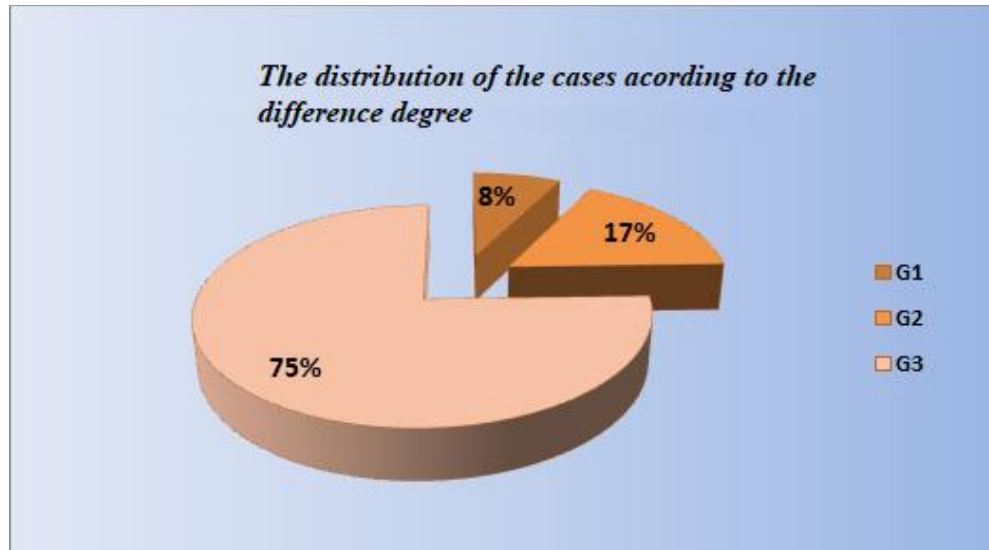


Figure 5 –The distribution of the cases according to the differentiation degree (Nottingham grading)

Microscopic analysis of surgical edges of surgical parts

The microscopical study of the surgical edges revealed the fact that in 38 cases (72%) the remains were negative, in 8 cases (15%) the remains/margins were positive, and in 7 cases (13%) the status of the margins remained unknown.

After establishing the certain diagnosis and the TNM stage, it was possible to establish the treatment through reciprocal collaboration between the surgeon, the oncologist and the radiotherapist, thus the therapeutical protocole was adjusted to each case.

The purpose, the place and the techniques of the surgical conservative treatment

The double purpose of conservative surgery is to obtain a good local control of the disease on long term and a minimum of local morbidity.

The selection of the patients for the use of conserving therapy was made following the indications and the contraindications of conserving surgery but also the particular cases taken separately. Some clinics have as a standard for the tumoral dimensions the limit of 3 centimetres of the tumor but in the Surgery Clinic of the Railway Clinical Hospital of Craiova, the conservative therapy is successfully made also for the tumors of 4 cm average, without any signs of local invasion.

The report between the tumoral dimension evaluated imagistically and the total volume of the breast is the one that dictates if the patient is suitable for conservative treatment. From this point of view it was noticed that if the patient has a bigger volume of mammary gland and the tumor is larger than 4 cm she is suitable for conservative surgery, while if the volume of the breast is small, even a small sectorectomy can have unacceptable cosmetic results.

The types of conservative surgical techniques which were used in the clinic:

- extended local excision (ELE) without axillary lymphadenectomy: in 8 cases;

- extended local excision + ipsilateral axillary lymphadenectomy: in 41 cases;
- quadrantectomy + ipsilateral axillary lymphadenectomy (LAI): in 3 cases.

Surgical treatment results:

The post-surgery evolution had the following results:

- a) *deaths* intra or post-surgery : in 0 cases;
- b) post-surgery *complications* (immediate and late) were represented by : hematoma, suppurating wounds, postoperative breast edema, arm lymphedema (swollen arm);

Immediate complications: (Figure 6)

1. *After surgery bleeding* – 2 cases (3,77%):

- 2 cases of postoperative prepectoral hematoma, for which interventions were made with the aim of hemostasis completion , with positive results;

2. *Wound suppurations* – 1 case (1,88%);

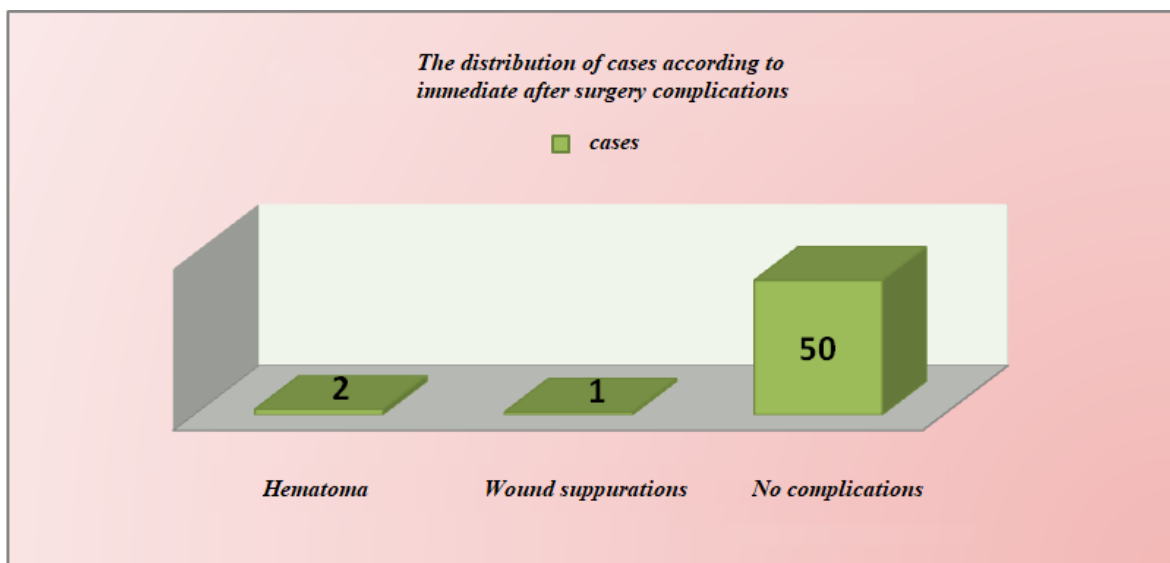


Figure 6: Case distribution according to immediate postoperative complications

Late complications: (Figure 7)

1. *Swollen arm* (after chronic edema) – appeared in 1 case (1,88%); the edema appeared gradually, becoming obvious 8 months after the surgery.

2. *Fake recurrences* – in 2 cases (3,77%):

- in one case an incompletely delimited tumor was discovered;
- 1 case of post surgery sanguinolent nipple discharge .

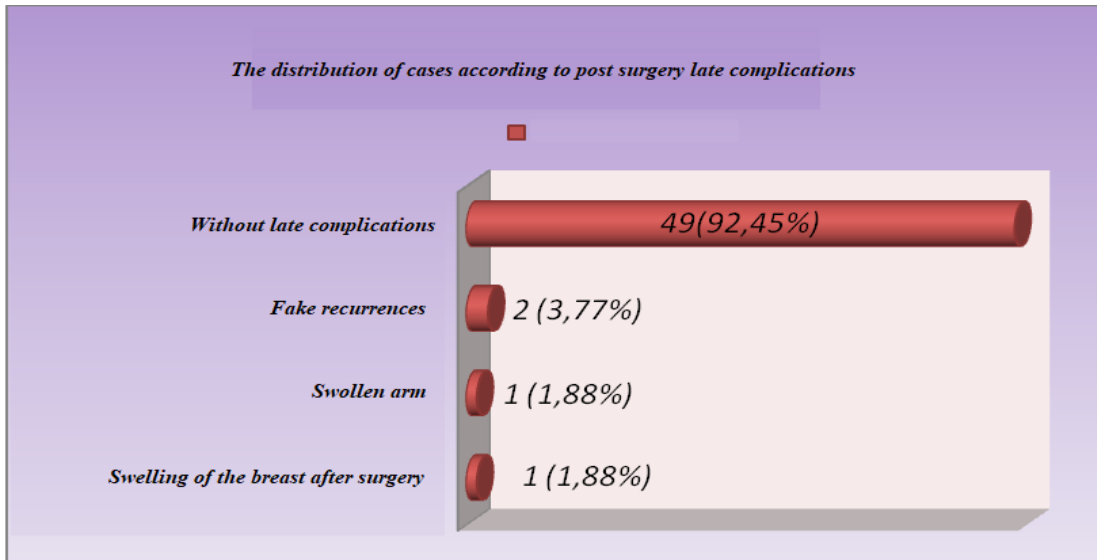


Figure 7 Cases distribution according to postoperative late complications

Recurrences

It is very well known that the number of recurrences is much higher in the case of conserving surgery in comparison with radical surgery, this fact being highlighted in the study group.

Real recurrences at the level of the operated breast were registered in 2 cases (3,77%). (Figure 8)

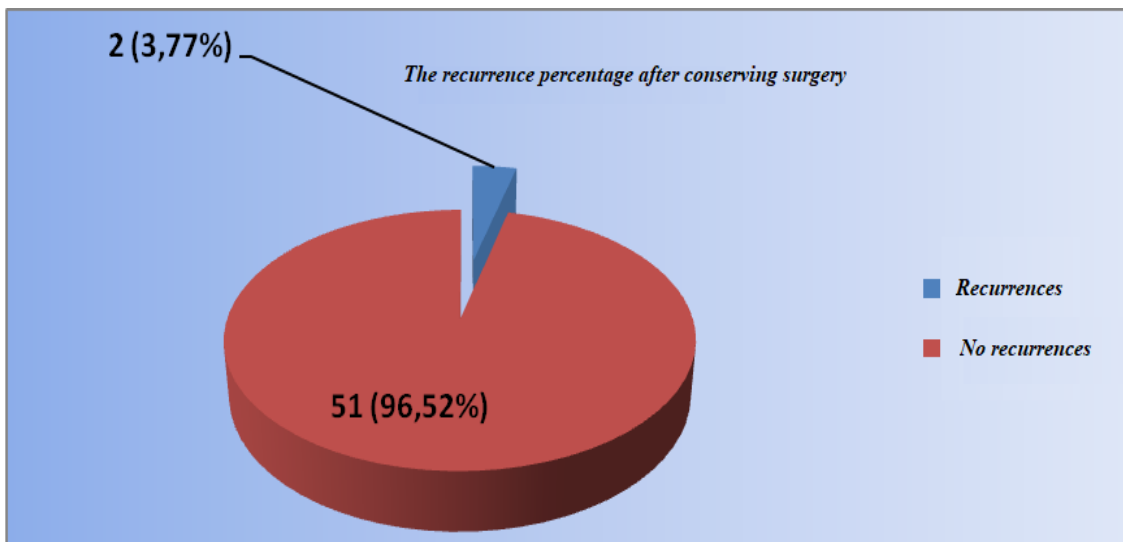


Figure 8 - The recurrence percentage after conserving surgery

It is necessary to mention the fact that, in these 2 cases the patients did not respect the treatment according to the protocols the patients have to follow after they were diagnosed (they did not benefit from radiotherapy).

The way to solve the 2 recurrences which appeared post conservatory surgery were:

- in one case we used sectorectomy.
- in the other case radical the patient asked for total mastectomy.

V. CONCLUSIONS

1. The surgical conservatory treatment of mammary neoplasm in stages I and II represent a good option after which the survival chances post surgery are the same as in mutilating surgery.
2. Apart from the patient's option, one of the most essential elements in applying conservative surgery is represented by the report between the volume of the tumor and the volume of the breast which has to be taken into consideration; such as the arbitrary decision of the maximum dimensions opted for in conserving surgery is excluded; what matters is obtaining an aesthetic result in maximum oncological safety regardless the dimension of the tumor, otherwise radical mastectomy is preferred followed by breast reconstruction.
3. Post surgery radiotherapy on the mammary gland is compulsory in order to get a satisfactory recurrence percent.
4. The complex oncological treatment applied post surgery can determine the conversion of some cases to the possibility of applying conservative surgery.
5. Conservative surgery in stages I and II must become "*the golden standard*" in the treatment of mammary cancer, because the results obtained over the years completely justifies this affirmation.
6. The age of the patients at the moment of the mammary tumor diagnosis is an important factor concerning ipsilateral recurrences which occurred; from this point of view we observed that the occurrence of ipsilateral recurrences is more frequently met at the patients under 40 years old in comparison with those who are over this age.
7. The improvement of the therapeutical results with the raise of life expectancy to 5 and 10 years and with the cost reduction of the treatment, can be obtained only by discovering the breast neoplasma at an early stage, which is possible through adopting and respecting screening programmes meant to discover the breast neoplasma as early as possible.

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REIRRADIATION FOR UNOPERATED RECTAL CANCER AFTER PRIOR PELVIC RADIATION THERAPY: A CASE REPORT

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Dragoș Eugen GEORGESCU³

ABSTRACT

INTRODUCTION: REGARDING PELVIC RECURRENCE OF UNOPERATED COLORECTAL CANCER, REIRRADIATION MAY BE AN OPTION FOR PATIENTS WHO STILL REFUSE SURGERY. COMORBIDITIES LIKE HIGH BODY-MASS-INDEX AND DIABETES HAS BEEN PROVEN TO BE UNFAVORABLE PROGNOSTIC FACTORS FOR PATIENTS WITH RECTAL CANCER. THE REPORT DESCRIBES
CASE DESCRIPTION: A 52 YEAR-OLD MAN KNOWN WITH TYPE 2 DIABETES MELLITUS AND DIAGNOSED IN 2012 WITH LOCALLY ADVANCED RECTAL ADENOCARCINOMA WHICH UNDERWENT NEOADJUVANT CHEMORADIOTHERAPY THAT REFUSED SURGERY. THE PATIENT ALSO REFUSED CHEMOTHERAPY REGIMENS, UNDERGOING ONLY CAPECITABINE SINGLE-AGENT THERAPY. FOLLOW-UP CT SCAN AND COLONOSCOPY IDENTIFIED LOCAL PROGRESSION AND, DUE TO PATIENT'S SURGERY REFUSAL, REIRRADIATION AND CONCURRENT CAPECITABINE BASED CHEMOTHERAPY WAS ADMINISTERED. REIRRADIATION WAS PERFORMED USING THE IMRT TECHNIQUE AND A HYPOFRACTIONATED RADIOTHERAPY REGIMEN. AT FOLLOW-UP CT SCAN A REDUCTION OF THE TUMORAL MASS WAS OBSERVED, WITH NO SIGNS OF METASTATIC DISEASE.
CONCLUSION: THIS CASE REPORT SUGGESTS THAT, IN VERY CAREFULLY SELECTED RECTAL CANCER PATIENTS, PELVIC RE-REIRRADIATION MIGHT BE AN OPTION FOR THOSE WHO REFUSE SURGERY.

KEYWORDS: CANCER, RECTUM, RADIOTHERAPY, CHEMOTHERAPY, REIRRADIATION

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INTRODUCTION

Despite survival rates are continually improving, colorectal cancer (CRC) is still a major cause of cancer morbidity and mortality worldwide⁴.

For locally advanced rectal cancer neoadjuvant chemoradiotherapy (NACRT)⁵ and resection radicality⁶ were the most important predictors for local recurrence and overall survival.⁷ Although for some patients complete response has been achieved following NACRT, current guidelines strongly recommend surgery following NACRT for rectal cancer patients with locally advanced disease.^{8,9} Sedentary lifestyle, western diet, obesity alongside other lifestyle and dietary risk factors for developing type 2 diabetes were associated with an increased risk of developing colorectal cancer.^{10,11,12} Current literature data are mainly suggesting a positive association between these two diseases, suggesting that diabetes might be a risk factor for developing colorectal cancer.^{13,14}

Herein, we report a case of a male patient diagnosed with locally advanced rectal cancer, known with multiple unfavorable prognostic factors including type 2 diabetes, who received 2 courses of radiotherapy to the pelvis, obtaining improved local control and OS, despite not undergoing radical surgery.

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CASE REPORT

A 52-year-old man known with type 2 diabetes mellitus and grade II obesity presented in April 2012 at the emergency with dyspnea, skin pallor and altered general condition and with a 3-month history of rectal bleeding. At digital rectal exam and colonoscopy (**Fig.3.A.1.**) a 6 cm x 4 cm tumor is identified in the lower rectum starting from the anal verge. Due to tumor friability a tumoral fragment detached and was sent to pathological examination which confirmed the diagnosis of a well differentiated tubular colorectal adenocarcinoma. Considering massive blood loss (haemoglobin (HGB) = 4.2 g/dl) inferior mesenteric artery embolization and multiple blood transfusions were performed, leading to an improvement of patients general condition and blood tests (HGB=10.4 g/dl).

Head-thorax-abdomen and pelvis computed tomography (CT) scan staging identified an inferior rectum locally invasive tumoral mass (**Fig.3.B.1.**) with bilateral internal iliac adenopathies. Given these results the disease was, based on American Joint Commission on Cancer (AJCC)¹⁵, stage IIIB (T3N1M0), therefore NACRT followed by radical surgery was the proposed treatment.

Radiotherapy was performed using a “4-field-box” (**Fig.1**) 3D conformal technique

to a total dose of 50 Grays (Gy) for a target volume including regional lymphnodes using a

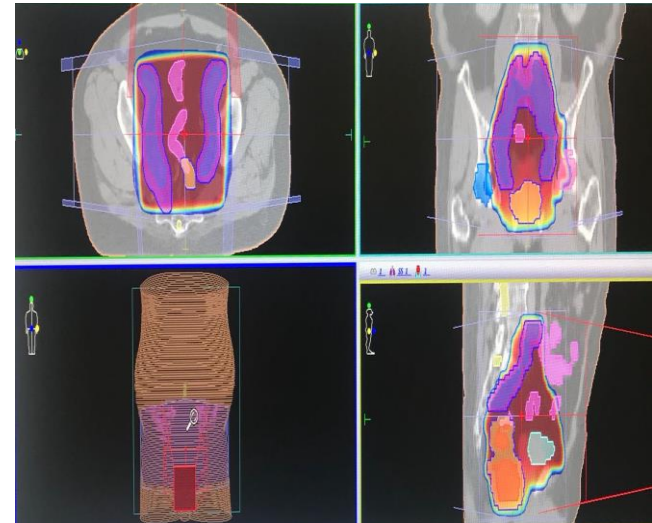


Fig.1 Initial pelvic radiotherapy using a 3D conformal “4-field-box” technique

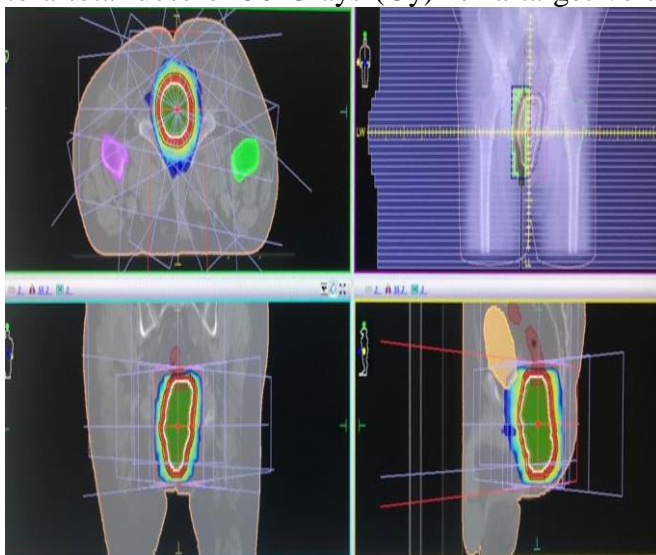


Fig.2 IMRT reirradiation treatment plan

conventional 2 Gy fractionation schedule. During radiotherapy fluoropyrimidine-based chemotherapy was administered with Capecitabine 825mg/m² twice daily, 5 days/week for 5 weeks. Follow-up CT scan and rectoscopy showed stationary disease, with no pelvic enlarged lymphnodes. Although radical surgery was proposed, the patient refused it, therefore the multidisciplinary tumor board for salvage 6 cycles of chemotherapy type CAPEOX with Oxaliplatin 130mg/m² day 1 and Capecitabine 1250 mg/m² twice daily days 1-14 every 3 weeks.

¹⁵ Colon and Rectum. In:Compton CC., Byrd DR., Garcia-Aguilar J., Kurtzman SH., Olawaiye A., Washington MK. (eds.) AJCC Cancer staging atlas, 2nd Ed. New York: Springer; 2012

The patient refuses Oxaliplatin treatment, therefore Capecitabine monochemotherapy is administered for six months.

Following six months of chemotherapy the patient presents with rectal bleeding, inability to completely empty the bowel and constipation, surgical and imaging exams (**Fig.3.A.2. and B.2.**) confirming a local progression of the disease. Surgery is proposed, but the patient refuses it for the second time therefore reirradiation is proposed. Intensity modulated radiotherapy (IMRT)(**Fig.2**) has been performed irradiating current tumor extension to a total dose of 36 Gy in 12 fractions using a 3 Gy/day fractionation schedule, administering by simultaneous integrated boost technique a radiation dose of 39 Gy for initial tumor extension using a 3.25 Gy/fraction schedule. During radiotherapy concurrent Capecitabine chemotherapy 825mg/m² twice daily, 5 days/week was administered. All symptoms were palliated after the starting from the 2nd treatment week, whilst patient tolerance was good, the only reported side effect being grade 3 proctitis and grade 2 rectalga. Following chemoradiotherapy, Capecitabine monochemotherapy 1250 mg/m² twice daily days 1-14 every 3 weeks was administered for eight months. At follow-up thorax-abdomen-pelvis CT scan (**Fig.3.B.3.**) asymmetrical parietal thickening of the lower rectum wall, with appearance in mild regression towards the previous CT exam was identified. Colonoscopy confirms the reduction of the lower rectum tumoral mass (**Fig.3.A.3.**).

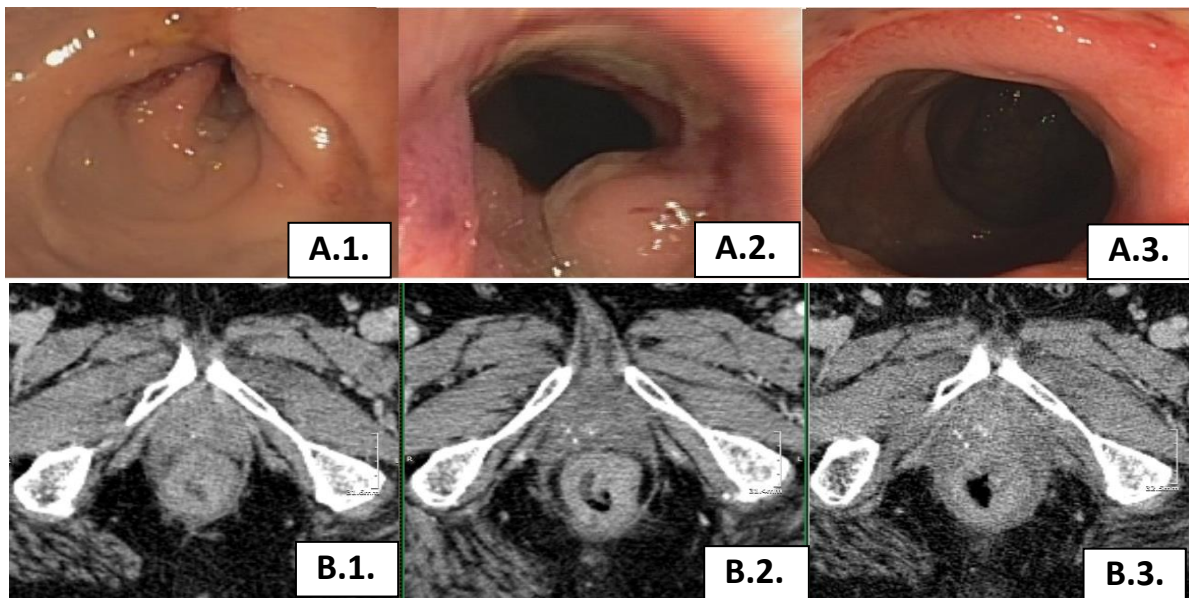


Fig.3. Colonoscopy (A.) and CT scan (B.) images at diagnosis (1.), relapse (2.) and at latest posttreatment follow-up (3.)

DISCUSSION

Current literature data strongly suggest a direct link between diabetes mellitus and colorectal cancer, most of these studies taking into account that diabetes mellitus might be considered an unfavorable prognostic factor for patients who develop colorectal cancer. In 2005 Larson SC. *et al.*¹⁴ performed a meta-analysis of fifteen studies with the purpose of finding a link between colorectal cancer and diabetes mellitus. Their results strongly support a connection between these two diseases in both women and men suggesting that hyperinsulinemia or insulin resistance might take part at the carcinogenetic process of colorectal cancer. Literature data suggest multiple links between diabetes mellitus and colorectal cancer. Therefore patient lifestyle focused studies suggest that both types 2 diabetes and colorectal cancer share risk factors like high body-mass-index (BMI) and sedentary lifestyle.^{13,16} Currently, although there are studies that consider diabetes mellitus an independent risk factor for colorectal cancer¹⁷, most epidemiological research data suggest that there are multiple connections between these two diseases which can be explained by certain biological processes like high levels of circulating C-peptide^{18,19}, insulin-like growth factor (IGF)-1^{20,21} and insulin²². Epidemiological data identified that for cancer patients comorbidities increase the need of a more complex therapeutic management, also decreasing disease free survival (DFS) and overall survival (OS) parameters.^{23,24} These data are not only related to diabetes mellitus, but also to high body-mass-index, which proved to be associated with an increased mortality rate compared to the normal weight category.²⁵ Regarding rectal cancer patients that didn't undergo surgery following neoadjuvant chemoradiotherapy, Lim *et al.*²⁶ identified a progression-free-survival (PFS) of 65

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²⁵ Flegal KM., Graubard BI., Williamson DF., Gail MH., Excess deaths associated with underweight, overweight, and obesity. *The Journal of the American Medical Association* 2005; 293(15): 1861-1867

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months for the complete response (CR) patients, compared to 15 months for the partial response (PR) ones. The same study identified that for stage T3 rectal cancer patients the median PFS was 28 months. T stage and clinical response were both considered predictors of PFS, but also that medical comorbidities and advanced age are unfavorable prognostic factors, reducing median overall-survival (OS) in rectal cancer patients who don't undergo surgery from 64 months to 27.5 months. Several literature data regarding rectal cancer reported high local recurrence rate even for complete responders not submitted for surgery within 3.7 to 8.8 months from chemoradiotherapy. Also, the same data suggest that adding brachytherapy to chemoradiotherapy did not improve PFS and OS.^{27,28} Regarding local recurrent rectal cancer that was previously irradiated multiple literature data suggest that reirradiation up to 30-40 Gy might be safe for palliation in resectable tumors.^{29,30,31} Prior studies regarding rectal cancer reirradiation^{30,32,33}, in which different radiotherapy schedules were used, concluded that the retreatment dose, and not the cumulative radiation dose, plays an important role for the OS rates of these patients. Therefore, by using a median cumulative dose of more than 30 Gy, OS rates of more than 20 months were achieved.³⁴ Although in most of these studies accelerated hyperfractionation radiation regimens were used, only *Nget al.*³³ published in 2013 the results of a study evaluating a once-daily reirradiation regimen for rectal cancer patients. This study concluded that reirradiation resulted in an 88% symptomatic response, but with poor OS rates of just 15 months for patients that didn't undergo radical surgery. The patient in this case report had multiple unfavorable individual prognostic factors like diabetes mellitus, dislipidemia and cardiac insufficiency. Besides that, more significant negative prognostic factors related to treatment were present such as refusing surgery and undergoing monochemotherapy with Capecitabine as systemic treatment. From our knowledge this is the only case of reirradiation of a patient with local relapse of rectal cancer without undergoing surgery or polichemotherapy regimens. PFS for our patient was comparable to previously reported data, but OS proves to be

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²⁸ Nakagawa WT., Rossi BM., Ferreira FD., et al. Chemoradiation instead of surgery to treat mid and low rectal tumors: is it safe? *Annals of Surgical Oncology* 2003;9(6): 568-573

²⁹ Glimelius B. Recurrent rectal cancer. The pre-irradiated primary tumor: Can more radiotherapy be given? *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland* 2003;5(5):501-503

³⁰ Mohiuddin M., Marks G., Marks J. Long-term results of reirradiation for patients with recurrent rectal carcinoma. *Cancer* 2002;95(5):1144-1150

³¹ Valentini V., Morganti AG., Gambacorta MA. et al. Preoperative hyperfractionated chemoradiation for locally recurrent rectal cancer in patients previously irradiated to the pelvis: A multicentric phase II study. *International journal of radiation oncology, biology, physics* 2006;64(4):1129-1139

³² Lingareddy V., Ahmad NR., Mohiuddin M. Palliative reirradiation for recurrent rectal cancer. *International journal of radiation oncology, biology, physics* 1997;38: 785-790

³³ Ng MK., Leong T., Heriot AG., Ngan SY. Once-daily reirradiation for rectal cancer in patients who have received previous pelvic radiotherapy. *Journal of medical imaging and radiation oncology* 2013; 57(4): 512-518

³⁴ Youssef FF., Parikh PJ., DeWees TA., Mutch MG., Tan BR., Grigsby PW., Myerson RJ., Olsen JR. Efficacy and toxicity of rectal cancer reirradiation using IMRT for patients who have received prior pelvic radiation therapy. *Advances in radiation oncology* 2016; 1(2): 94-100

higher than in these studies. Although there were data that reported even a third reirradiation³⁵, from our knowledge this is the first case describing a hypofractionated regimen of reirradiation for a recurrent rectal cancer. Current reported data suggested increased grade 3 and 4 gastrointestinal toxicity, but also lumbosacral plexopathy following the second reirradiation, but this is not applicable to our patient, probably due to the reirradiation of a target volume limited to the relapsed tumor and not of the whole pelvis.

³⁵ Tao R., Tsai CJ., Das P. et al. Hyperfractionated accelerated reirradiation for rectal cancer: An analysis of outcomes and toxicity. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology* 2017; 122(1): 146-151

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RECURRENT RECTAL CANCER COMPLICATED WITH PERFORATION AND NECROTISING FASCIITIS DURING NEOADJUVANT THERAPY

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ABSTRACT:

INTRODUCTION: RECTAL CANCER LOCAL RECURRENCE IS LESS FREQUENT SINCE MULTIDISCIPLINARY APPROACH HAS BEEN IMPLEMENTED, USUALLY TME EXCISION BEING PERFORMED AFTER NEOADJUVANT THERAPY. IN CASE OF RECURRENCE, NEOADJUVANT THERAPY, INCLUDING STANDARD DOSE RADIOTHERAPY SHOULD BE CONSIDERED IF NOT PERFORMED INITIALLY. PATIENTS PREVIOUSLY IRRADIATED, CAN BENEFIT OF LOWER-DOSES RE-IRRADIATION CONCOMITANT WITH CHEMOTHERAPY, FACILITATING A CURATIVE SURGICAL RESECTION.

CASE REPORT: IT IS PRESENTED THE CASE OF A 68 YEARS OLD PATIENT, WHO PERFORMED A RECTAL ANTERIOR RESECTION WITH COLO-RECTAL ANASTOMOSIS FOR RECTAL TUMOR 4 YEARS BEFORE IN ANOTHER MEDICAL UNIT. THE PATIENT IS DIAGNOSED WITH RECURRENCE INVOLVING THE ANASTOMOSIS, FOR WHICH MULTIDISCIPLINARY TEAM RECOMMENDED RADIOCHEMOTHERAPY PRIOR TO SURGERY. DURING THE NEOADJUVANT THERAPY, BEFORE THE LAST CHEMOTHERAPY CURES THE PATIENT IS EMERGENCY SUBMITTED TO SURGERY SERVICE FOR INFLAMMATORY TUMEFACATION WITH NECROTISING FASCIITIS IN THE RIGHT ISCHIORECTAL FOSSA. A FIRST SURGERY CONSISTING IN DRAINAGE AND EXTENSIVE DEBRIDEMENT ALSO OBSERVES RECTAL WALL PERFORATION. A SECOND IMMEDIATE INTERVENTION CONSISTING IN A TERMINAL COLOSTOMY IS PERFORMED. AFTER ANTIBIOTHERAPY, LOCAL DRESSINGS, AND SEPTIC CONTROL OF THE WOUND AN ABDOMINO-PERINEAL SALVAGE RESECTION IS DONE, AN IMPORTANT SKIN DEFECT REMAINING.

CONCLUSION: A QUICK AND EFFICIENT MANAGEMENT OF A SEVERE CONDITION PERMITTED NOT ONLY TO CONTROL A LIFE THREATENING SITUATION, BUT ALSO PERFORMING AN ABDOMINO-PERINEAL RESECTION. A MORE OFTEN OR MAYBE ROUTINELY USE OF DIVERTING COLOSTOMY BEFORE RADIOCHEMOTHERAPY SHOULD BE CONSIDERED IN CASE OF RECURRENT RECTAL CANCER, DETAILED STUDIES BEING NECESSARY ON THIS ASPECT.

KEY WORDS: RECTUM, CANCER, RECURRENCE, PERFORATION, RADIOCHEMOTHERAPY

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INTRODUCTION

Multimodality of treatment, the use of neoadjuvant radiochemotherapy in combination with TME (total mesorectal excision) decreased rectal cancer local recurrence dramatically, to an average of about 5% according to some studies⁵. Surgery of recurrent disease has become more difficult after the introduction of TME concept and preoperative radio and chemotherapy⁶. A curative resection remains though the aim of treatment for recurrent rectal cancer, as a macroscopic residual disease cannot be compensated by radio or chemotherapy⁷. Curative resection may be facilitated by re-irradiation to lower doses concomitant with chemotherapy in previously irradiated patients⁸. Current literature data are mainly suggesting that diversion is unnecessary in endoscopically obstructed rectal cancer without clinical signs of obstruction, immediate initiation of neoadjuvant chemoradiotherapy being safe and feasible⁹. Herein we report a case of a male patient diagnosed with locally advanced recurrent rectal cancer who received neoadjuvant radio chemotherapy to facilitate radical curative surgery, but during therapy the case complicated with perforation and necrotising fasciitis.

CASE REPORT

A 68 years old male patient is emergency submitted for inflammatory tumefaction with necrotising fasciitis located in the right ischioanal fossa, associating sepsis, asthenia, fever and chills, diarrhoea.

From patients medical history we record that he was previously diagnosed with recurrent locally advanced rectal cancer, for which neoadjuvant radio chemotherapy has been initiated according to the multidisciplinary board decision. The initial rectal tumour located in the medium rectum, at approximately 10 cm from the anal verge (well differentiated adenocarcinoma) was treated with rectal resection and colorectal anastomosis (pT2pN0G2) followed by adjuvant radiotherapy (45 Gy) and chemotherapy. Follow up at 3, 6 9 months, at one year and two years observes no signs for recurrent disease at digital rectal examination colonoscopy, ecography or CT scan, tumoral markers CEA and CA19.9 being in normal range. Another colonoscopy performed at about 3 years from initial surgery suggests tumour recurrence, from 6 to 18 cm, including the anastomosis, biopsies being taken. The histopathological findings show G3 rectal adenocarcinoma. A thorax and abdominal CT scan and a pelvic MRI are performed. The results show locally advanced obstructive rectal cancer recurrence, mesorectal lymph nodes and 2 hepatic micronodules with secondary aspect.

⁵ Sebag-Montefiore, D, Stephens, RJ, Steele, R et al, M. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG CO 16): a multicentre, randomised trial. *Lancet*. 2009;373:811–820.

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⁷ Huh JW. Curative potential of surgical resection for locally recurrent rectal cancer. *Ann Surg*. 2014 Jun;259(6):e88.

⁸ Guren MG, Undseth C, Rekstad BL et al. Reirradiation of locally recurrent rectal cancer: a systematic review. *Radiother Oncol* 2014; 113: 151–157.

⁹ Patel JA, Fleshman JW, Hunt SR, Safar B, Birnbaum EH, Lin AY, Mutch MG. Is an elective diverting colostomy warranted in patients with an endoscopically obstructing rectal cancer before neoadjuvant chemotherapy? *Dis Colon Rectum*. 2012 Mar;55(3):249-55

The multidisciplinary team proposes neoadjuvant polichemoyherapy (PCT), re-irradiation to lower doses, followed by curative surgery. Chemotherapy with fluorouracil (5-FU) and calcium folinate associated with bevacuzimab has been initiated. Under chemotherapy a febrile episode associated with chills was interpreted as paraneoplastic syndrome. Photon beam radiation therapy (VMAT tehniqe) has been performed irradiating current tumor extension to a total dose of 30 Gy in 10 fractions using a 3 Gy/day fractionation schedule. Imagistic and colonoscopy reevaluation showed slight regression of tumour and no pulmonary or hepatic metastasis on MRI and CT scan and an ulcerative rectal tumor starting at 4 cm from the anal verge with possible fistulary orifices. Afterwards PCT has been continued and before the last session the patient was emergency admitted to surgery for septic syndrome and inflammatory tummefaction with necrotising fasciitis located in the right ischioanal fossa, extended to the right scrotal area (Fig.1), associating asthenia, fever and chills, diarrhoea, but no abdominal pain or signs of peritoneal irritation. Emergency surgery has been performed consisting in incision, drainage of fecals and pus (Fig.2.A), and extensive debridement (Fig2.B). A probe for bacteriological examination and antibogram has been taken, antibiotherapy being administered conformly with the results (*Pseudomonas Spp* - Colistine + Metronidazole). Additional *Candida Spp* has been found and treated with fluconazole.



Figure 1. Inflammatory tummefaction with necrotising fasciitis



Figure 2. (A) Incision. Drainage of pus and fecals. (B) Aspect after debridement. (C) Rectal wall perforation

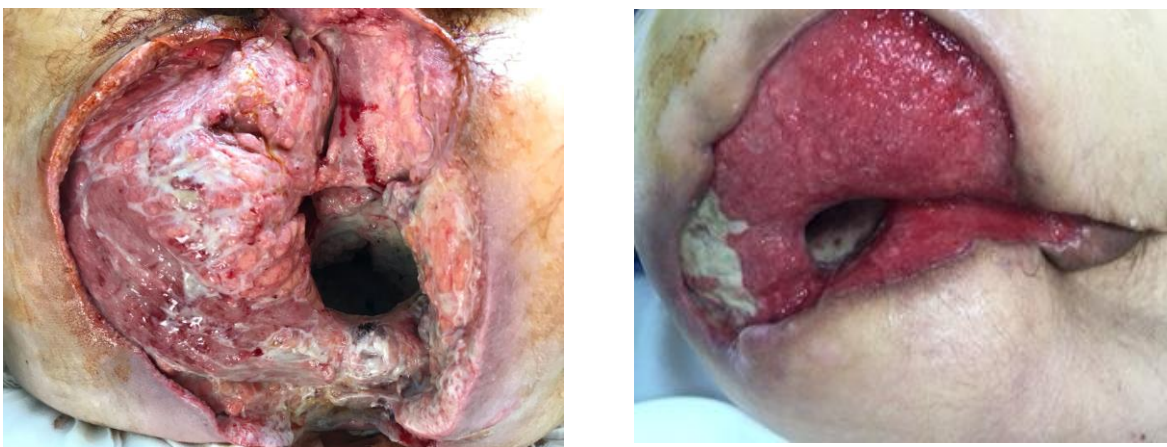


Figure 3. (A) Aspect after abdomino-perineal resection (B) Aspect at 1 month after discharge

Important rectal wall perforation has been noticed (Fig.2C) and a second intervention consisting in a terminal colostomy became mandatory. Postoperative evolution was favourable and permitted after 2 weeks an abdomino-perineal resection (Fig.3.A). The patient has been discharged with good status, granulated perineal wound, with important skin loss. The histopathological result surprisingly showed chronic inflammatory infiltrate, fibrosis and necrosis areas, but no malignant cells.

DISCUSSIONS

Regarding pretherapeutical assessment, imaging can establish the local extent of the tumour and can detect distant metastases. Current literature data suggest that approximately 50% of the patients with local recurrence have detectable distant metastases at the time of diagnoses¹⁰. Some studies consider the cases with distant metastases present in the initial evaluation unsuitable for curative treatment¹¹. In this particular case, there were two liver micrododules with secondary aspect described on initial abdominal CT scan. After neoadjuvant chemotherapy, imagistic reassessment showed no distant pulmonary or liver metastases.

- Even though MRI is useful in assessing local recurrence, DWI-MRI (*Diffusion Weighted Imaging*) is being able to distinguish better tumour from scar tissue^{12,13,14,15} PET-scan has also been useful, especially in finding unsuspected metastatic disease¹⁶.

- Despite the fact that many surgeons prefer immediate diversion in patients with endoscopically obstructed rectal cancer before starting neoadjuvant chemotherapy, current literature data shows that immediate diversion is unnecessary in endoscopically obstructed rectal cancer without clinical signs of obstruction. Diverting colostomy delays the initiation of neoadjuvant chemoradiotherapy and proctectomy^{17,18} In this particular case the use of a diverting colostomy before initiation of neoadjuvant radiochemotherapy would have not prevented the rectal wall perforation, but would have protected the patient from the consecutive necrotising

¹⁰ Wiggers T Management of local recurrence of rectal cancer. *European Journal of Cancer*, September 2011, Volume 47, Supplement 3, Pages S290–S291

¹¹ van den Brink, M, Stiggelbout, AM, van den Hout, WB et al, Clinical nature and prognosis of locally recurrent rectal cancer after total mesorectal excision with or without preoperative radiotherapy. *J Clin Oncol*. 2004;22:3958–3964.

¹² Salerno G et al. Defining the rectum: surgically, radiologically and anatomically. *Colorectal Dis*. 2006;8 Suppl 3:5–9

¹³ Kim DJ, Kim JH, Lim JS, et al. Restaging of rectal cancer with MRI imaging after concurrent chemotherapy and radiation therapy. *Radio Graphics* 2010;30:503–16

¹⁴ Dzik-Jurasz A, Domenig C, George M, et al. Diffusion MRI for prediction of response of rectal cancer to chemo radiation. *Lancet* 2002;360:307–8

¹⁵ Rania A. Marouf, Mary Y. Tadros, Tarek Y. Ahmed. Value of diffusion-weighted MR imaging in assessing response of neoadjuvant chemo and radiation therapy in locally advanced rectal cancer. *The Egyptian Journal of Radiology and Nuclear Medicine*. Volume 46, Issue 3, September 2015, Pages 553–561

¹⁶ Franke, J, Rosenzweig, S, Reinartz, P et al, Value of positron emission tomography (18F-FDG-PET) in the diagnosis of recurrent rectal cancer. *Chirurg*. 2000;71:80–85

¹⁷ Kaiser AM. Diversion with neoadjuvant vs surgery with adjuvant treatment for obstructing rectal cancer? *Dis Colon Rectum*. 2012 Oct;55(10):e346

¹⁸ National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), *Rectal Cancer, Version 4.2017* - January 18, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/rectal.pdf on February 8, 2018

fasciitis and from a life threatening situation. Even more, considering that surgery is the only curative treatment in patients with locally recurrent rectal cancer¹⁹, the severe septic complication threatened the tumor-free resection margin (R0) and the overall survival (OS).

Although bowel perforation has been reported before as a serious side effect of bevacuzimab in a limited number of cases, its association with fasciitis its rare²⁰. In the presented case, bevacuzimab was associated with 5-FU and calcium folinate.

Current treatment for locally advanced rectal cancer, including neoadjuvant therapy and total mesorectal excision lead to considerably fewer recurrences. In case of recurrent rectal cancer, if RT has not already been given, patients should be considered for standard-dose, preoperative CRT (45–50 Gy in 5–6 weeks)²¹ or short course preoperative radiotherapy followed by a fluoropyrimidine and oxaliplatin-based chemotherapy²² prior to an attempt of resection.

In patients previously irradiated, re-irradiation to lower doses with concomitant chemotherapy is safe and can be used in selected patients to facilitate a curative resection or per se to palliate symptoms. In the reported case, the patient was initially irradiated after the primary rectal resection, adjuvant radiotherapy being administered (45 Gy). In consequence, the multidisciplinary team considerate neoadjuvant re-irradiation to a total dose of 30 Gy in 10 fractions using a 3 Gy/day fractionation schedule.

CONCLUSIONS

A prompt and efficient surgical attitude allowed a good therapeutical control in a life threatening situation, and also permitted an abdomino-perineal resection with surprisingly satisfying histopathological result. A more often or maybe routinely use of diverting colostomy before neoadjuvant therapy should be considered in case of recurrent rectal cancer, especially when re-irradiation and polichemotherapy associated with bevacuzimab are taken into consideration.

¹⁹Selvaggi F1, Fucini C, Pellino G, Sciaudone G, Maretto I, Mondì I, Bartolini N, Caminati F, Pucciarelli S. Outcome and prognostic factors of local recurrent rectal cancer: a pooled analysis of 150 patients. *Tech Coloproctol*. 2015 Mar;19(3):135-44. doi: 10.1007/s10151-014-1241-x. Epub 2014 Nov 11.

²⁰Shimada A1, Nakamura T, Ishii M, Chiba N, Ishikawa S, Arisawa Y, Hashimoto M. A case of necrotizing fasciitis developed in a patient with recurrent rectal cancer treated with chemotherapy [Article in Japanese] *Gan To Kagaku Ryoho*. 2013 May;40(5):663-5.

²¹Braendengen M, Tveit KM, Berglund A et al. Randomized phase III study comparing preoperative radiotherapy with chemoradiotherapy in nonresectable rectal cancer. *J Clin Oncol* 2008; 26: 3687–3694.

²²Bujko K, Wyrwicz L, Rutkowski A et al. Long-course oxaliplatin-based preoperative chemoradiation versus 5 x5Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study. *Ann Oncol* 2016; 27: 834–842.

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THE ROLE OF ALUMINUM IN THE SYMPTOMATOLOGY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN

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ABSTRACT

ALUMINUM IS A CHEMICAL ELEMENT ATOMIC NUMBER 13. IT IS WHITE-SILVER, INSOLUBLE IN WATER UNDER NORMAL CONDITIONS. DESPITE ITS NATURAL ABUNDANCE, ALUMINUM HAS NO KNOWN BIOLOGY FUNCTION. IT IS A TOXIC RESIDUE, ALUMINUM SULPHATE HAVING AN LD50 OF 6207 MG/KG BODY, CORRESPONDING TO 500 GRAMS PER 80 KG PERSON. EXTREMELY ACUTE TOXICITY WITHOUT HARM TO HEALTH IS OF INTEREST IN VIEW OF THE WIDESPREAD OCCURRENCE OF THE ELEMENT IN THE ENVIRONMENT AND IN TRADE⁷. TOXICITY CAN BE TRACKED AFTER DEPOSITION INTO THE BONES AND THE CENTRAL NERVOUS SYSTEM AND IS PARTICULARLY HIGH IN PATIENTS WITH RENAL INSUFFICIENCY. BECAUSE ALUMINUM COMPETES WITH CALCIUM FOR ABSORPTION, INCREASED ALUMINA CAN CONTRIBUTE TO OSTEOPENIA, PRETERM AND GROWTH RETARDATION. IN VERY HIGH DOSES, ALUMINUM CAN CAUSE NEURO TOXICITY ASSOCIATED WITH ALTERED FUNCTION OF THE BLOOD-BRAIN BARRIER⁸.

OBJECTIVES

THE STUDY PROPOSES A COMPARISON OF THE CONCENTRATION OF URINE ALUMINUM HARVESTED FROM A GROUP OF CHILDREN DIAGNOSED WITH ADHD VERSUS THE NORMAL "CHILDREN'S HOMES SOS CHILDREN'S VILLAGES" AND THE ANALYSIS OF THE INFLUENCE OF THE SEX OF THE CHILDREN ON URINE CONCENTRATIONS OF ALUMINUM.

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⁷ Helmboldt O. Aluminum Compounds, Inorganic. Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH, 2007

⁸ Banks W.A., Kastin A.J. Aluminum-induced neurotoxicity: alterations in membrane function at the blood-brain barrier. Neurosci Biobehav Rev, 1989, 13 (1): 47-53

DETERMINATION OF THE URINARY CONCENTRATION OF ALUMINUM, PERFORMED BY THE ATOMIC ABSORPTION SPECTROMETER WITH ATOMIZATION IN GRAPHITE FURNACE TECHNIQUE (GF-AAS)⁹. WAS USED TO DETERMINE THE ALUMINUM CONCENTRATION IN THE INJECTION MATRIX.

CONCLUSIONS

THERE IS NO SIGNIFICANT DIFFERENCE BETWEEN THE AVERAGE URINE CONCENTRATIONS OF THE TWO GROUPS OF NORMAL CHILDREN AND THE SYMPTOMS OF ADHD.

IT CAN BE ARGUED THAT THE OCCURRENCE OF SYMPTOMATIC SYMPTOMS CHARACTERISTIC OF ADHD CAN NOT BE CORRELATED WITH THE PRESENCE OF ABNORMAL VALUES OF ALUMINUM IN SUBJECTS WITH ADHD.

THE ANALYSIS OF ALUMINUM URINE CONCENTRATIONS IN CHILDREN WITH ADHD RELATIVE TO THE URINARY CONCENTRATION OF THESE ELEMENTS IN CHILDREN WITHOUT ADHD DID NOT REVEAL ANY STATISTICALLY SIGNIFICANT DIFFERENCE. THESE RESULTS SHOW THAT ALUMINUM CAN NOT BE RESPONSIBLE FOR THE PRESENCE OF ADHD SYMPTOMS.

THE DEVELOPED OPTOELECTRONIC METHOD IS RELATIVELY SIMPLE, REPRODUCIBLE AND HAS A SENSITIVITY THAT ALLOWS ANALYSIS OF THE COBALT CONCENTRATION IN THE URINE SAMPLES.

KEY WORDS: ADHD, URINE, ALUMINIUM, GF-AAS

INTRODUCTION

Aluminum is a chemical element atomic number 13. It is white-silver, insoluble in water under normal conditions. It is a common chemical element, occupying the third position, after oxygen and silicon, SD a terrestrial spread of 7.4%. Aluminum compounds make up 8.13% of the earth's crust, being found in mineral substances SD well SD in the plant and animal world. It is naturally occurring in the form of minerals, silico aluminates (feldspar, small clays), cryolite (sodium fluoaluminate), bauxite, and corindone. After iron, it became the most widely used metal. Aluminum was noted for being a lightweight metal with a density of 2.7 g/cm³. This quality makes it used in large quantities in the naval and aeronautical industries. High reflectivity is used in the construction of metal mirrors¹⁰. Aluminum is remarkable for its low metal density and its ability to withstand corrosion. Despite its prevalence in the environment, aluminum salts are not known to be used by any form of life. According to its omnipresence, aluminum is well tolerated by plants and animals¹¹.

Aluminum is durable, ductile and malleable, with looks ranging from silver to gray matte, depending on the surface roughness. It is non-magnetic and does not light easily. Aluminum alloys have yield strength ranges ranging from 200 MPa to 600 MPa¹². Aluminum

⁹ Ionică M. Dispozitive optoelectronice pentru măsurarea radiației electromagnetice ultraviolete, vizibile sau infraroșii. Curs anul II masterat Optoelectronică 2017/2018, Departamentul Tehnologie Electronică și Fiabilitate, Facultatea de Electronică Telecomunicații și Tehnologia Informației, Universitatea „Politehnica” din București; Davițoiu A.M. Bărcănescu Ș., Negulescu V.Al., Avram O., Voicu V.A., Macovei R., Tudosie M., Caragea G., Forje M., Mladin C., Fragkos A., Ardelean L., Bumbea V. Selenium removal study in patients with chronicrenal disease. Therapeutics pharmacology and clinical toxicology, December 2013, Vol. XVII: 167-177

¹⁰ Shakhashiri B.Z. Chemical of the Week: Aluminum. *SciFun.org*. University of Wisconsin, 17 March 2008

¹¹ Helmboldt O. Aluminum Compounds, Inorganic. Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH, 2007

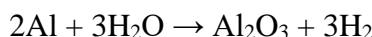
¹² Polmear I.J. Light Alloys: Metallurgy of the Light Metals (3rd ed.). Butterworth-Heinemann, 1995

has about one-third of the density and stiffness of the steel. It is easy to process, cast, draw and extrude.

Aluminum atoms are arranged in a cubic-centered structure. Aluminum has a stacking energy of approximately 200 MJ/m^2 ¹³. Aluminum is a good thermal and electric conductor, having 59% of the conductivity of copper both thermally and electrically, with only 30% of the copper density. Aluminum is capable of being a superconductor with a critical superconductor temperature of 1.2 Kelvin and a critical magnetic field of about 100 Gauss (10 mT)¹⁴.

CHEMICAL PROPERTIES

Corrosion resistance can be excellent due to a thin layer of aluminum oxide that forms when the metal is exposed to air, effectively preventing oxidation. The strongest aluminum alloys are resistant to corrosion due to galvanic copper alloy reactions¹⁵. Due to the corrosion resistance, aluminum is one of the few metals that retain silver reflection in the form of fine dust. Aluminum is oxidized by water to produce hydrogen and heat:



This conversion is of interest to hydrogen production. The formed oxide layer inhibits the storage of the energy of the regeneration of metals¹⁶.

ALUMINUM ISOTOPES

Aluminum has many known isotopes, only ²⁷Al (stable isotope) and ²⁶Al (radioactive isotope, $t_{1/2} = 7.2 \times 10^5$ years) occur naturally. ²⁷Al has a natural abundance of over 99.9%. ²⁶Al is produced from argon. The ratio between ²⁶Al and ¹⁰Be was used to study the role of transport, deposition, sediment storage and erosion over time¹⁷. Meteorite research has shown that ²⁶Al was relatively abundant when it was planetary. Most scientists believe that the energy released by meteorites through ²⁶Al disintegration was responsible for melting and differentiating asteroids 4.5 billion years ago¹⁸.

THE BIOLOGICAL ROLE OF ALUMINUM

Despite its natural abundance, aluminum has no known biology function. It is a remarkable toxic, aluminum sulfate having an LD50 of 6207 mg/kg (oral dose) corresponding to 500 grams per 80 kg person. Extremely acute toxicity without harm to health is of interest in view of the widespread occurrence of the element in the environment and in trade¹⁹. Toxicity can be tracked after deposition into the bones and the central nervous system and is particularly

¹³ Dieter G.E. Mechanical Metallurgy. McGraw-Hill, 1988

¹⁴ Cochran J.F., Mapother D.E. Superconducting Transition in Aluminum. Physical Review 111 (1): 132–142. Bibcode 1958 PhRv: 111-132C

¹⁵ Cochran J.F., Reaction of Aluminum with Water to Produce Hydrogen. U.S. Department of Energy. January 1, 2008

¹⁶ Dickin A.P. In situ Cosmogenic Isotopes. Radiogenic Isotope Geology. Cambridge University Press. 2005

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¹⁸ Dodd R.T. Thunderstones and Shooting Stars. Harvard University Press. 1986: 89–90

¹⁹ Shakhshiri B.Z. Chemical of the Week: Aluminum. *SciFun.org*. University of Wisconsin, 17 March 2008

high in patients with renal insufficiency. Because aluminum competes with calcium for absorption, increased amounts of aluminum can contribute to osteopenia in preterm and growth retarded children. In very high doses, aluminum can cause neuro toxicity associated with altered function of the blood-brain barrier²⁰. A small percentage of people are allergic to aluminum. Other issues are related to contact dermatitis, digestive disorders, vomiting, or other symptoms when contacting or ingesting products containing aluminum, such as deodorants or antacids. Seafaring personnel, who come into direct contact with aluminum through the nature of the profession, have not been found to have any higher values than the average population²¹. In non-allergic patients, aluminum is not as toxic as other metals, but there is some evidence of toxicity if consumed in excessive amounts²². In patients with chronic renal disease, due to modification of dialysis technology, aluminum contamination of the dialyzer was significantly reduced²³. Although the use of aluminum cans has not been shown to be harmful, in general, excessive use of antacids with aluminum compounds offers several significant levels of exposure.

Studies have shown that the consumption of acidic foods or fluids in aluminum vessels increases significantly the absorption of aluminum²⁴. Furthermore, aluminum increases estrogen secretion associated with gene expression in neoplastic breast cells²⁵. These effects have led to their classification as metalloestrogens.

The effects of aluminum in antiperspirants have been examined for decades, with little evidence of skin irritation²⁶. There is little evidence that normal exposure to aluminum poses a risk to healthy adults²⁷. There are also studies on the risks associated with increased exposure to metal²⁸. Aluminum in food can be absorbed more from water²⁹. The role of aluminum as a

²⁰ Helmboldt O. Aluminum Compounds, Inorganic. Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH, 2007

²¹ Ionică M., Macovei R., Caragea G., Dănescu I. Aluminium levels determination by GF-AAS for aircraft employees. 45th Congress of the European Societies of Toxicology, 05-08 octombrie 2008, Rhodes, Greece. TOXICOLOGY LETTERS, vol. 180, Supplement 1: S128-S129; Ionică M., Voicu V., Rusea D., Macovei R., Caragea G., Forje M. Urine aluminium levels in airport technical involved employees. Balkan Military Medical Committee 10th Anniversary Congress, 2-6 octombrie 2005, Varna, Bulgaria

²² Abreo V. The Dangers of Aluminum Toxicity. Archived from the original on 18 April 2009

²³ Păun S.C., Tudose M.S., Macovei R., Ardelean Luminița, Bumbea Viorica, Caragea Genica, Ionică M., Mircioiu C., Piperea-Sianu A., Mladin C. Evaluation and modeling of kinetics of aluminium in plasma and dialysis fluid. Therapeutics, Pharmacology and Clinical Toxicology Vol XVI, Number 4, December 2012: 269 – 273

²⁴ Slanina P., French W., Ekström L.G., Löf L., Slorach S., Cedergren A. Dietary citric acid enhances absorption of aluminum in antacids. Clinical Chemistry (American Association for Clinical Chemistry), 1986, 32 (3): 539–541; Van Ginkel M.F., Van Der Voet G.B., D'haese P.C., De Broe M.E., De Wolff F.A. Effect of citric acid and maltol on the accumulation of aluminum in rat brain and bone. The Journal of laboratory and clinical medicine, 1993, 121 (3): 453–60

²⁵ Darbre P.D. Metalloestrogens: an emerging class of inorganic xenoestrogens with potential to add to the oestrogenic burden of the human breast. Journal of Applied Toxicology, 2006. 26 (3): 191–7

²⁶ Shakhshiri B.Z. Chemical of the Week: Aluminum. *SciFun.org*. University of Wisconsin, 17 March 2008

²⁷ Gitelman H.J. Physiology of Aluminum in Man, in Aluminum and Health, CRC Press, 1988

²⁸ Ferreira P.C., Piai Kde A., Takayanagui A.M., Segura-Muñoz Aluminum as a risk factor for Alzheimer's disease. Revista Latino-americana de enfermagem, 2008, 16 (1): 151–7

²⁹ Yokel R.A., Hicks C.L., Florence R.L. Aluminum bioavailability from basic sodium aluminum phosphate, an approved food additive emulsifying agent, incorporated in cheese. Food and chemical toxicology, 2008, 46 (6): 2261–6

factor in Alzheimer's disease is controversial³⁰. According to the Alzheimer Society, studies have not convincingly demonstrated a causal relationship between aluminum and Alzheimer's disease³¹. However, some studies such SD those on the PAQUID cohort cite exposure to aluminum SD a risk factor for Alzheimer's disease. Some brain plates have been found with high levels of aluminum³².

In any case, if there is no toxicity of aluminum, this aspect must be linked to a very specific mechanism, because the total human exposure of the clay-dust element to the natural soil is extremely high. There is no scientific consensus on the possibility that exposure to aluminum may directly increase the risk of Alzheimer's disease³³.

OBJECTIVES

The study aims to make a comparison between the concentrations of urine from the batch of children diagnosed with ADHD compared to those in the “*Children's House SOS Children's Villages*” and to analyze the influence of the sex of the children on the urinary concentrations of aluminum. Determination of the urinary concentration of aluminum was done by the atomic absorption spectrometer with atomization in graphite furnace, (GF-AAS)³⁴.

MATERIAL AND METHOD

The study was conducted between 2013 and 2014 at the “Children's home - SOS Children's Villages” on a 50-child group divided into two groups:

- A group, consisting of 25 children without ADHD, Sex repatriation was: 12 boys and 13 girls;
- B group of 25 children with ADHD, broken down by sex SD follows: 14 boys and 11 girls.

The criteria for inclusion of children in A group were:

- age between 7 and 15 years.

Criteria to exclude children in A group:

- the existence of psychiatric diagnosis (mental deficiency, autism, psychosis, etc.);
- the existence of chronic neurological diseases: paresis, infantile brain paralysis, etc.

Criteria for inclusion of children in B group:

- ages 7 to 15;
- ADHD diagnosis: hyperkinetic disorder accompanied by attention deficit, hyperkinetic disorder accompanied by impulsivity;

³⁰ Ferreira P.C., Piai Kde A., Takayanagui A.M., Segura-Muñoz Aluminum SD a risk factor for Alzheimer's disease. *Revista Latino-americana de enfermagem*, 2008, 16 (1): 151–7

³¹ Yokel R.A., Hicks C.L., Florence R.L. Aluminium and Alzheimer's disease, The Alzheimer's Society. Retrieved 30 January 2009.

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³⁴ Polmear I.J. *Light Alloys: Metallurgy of the Light Metals* (3rd ed.). Butterworth-Heinemann, 1995; Dieter G.E. *Mechanical Metallurgy*. McGraw-Hill, 1988

- duration of pharmacological treatment prior to inclusion in the group, less than or equal to 6 months;

- the possibility of following outpatient treatment.

Sex was not a selection criterion.

Criteria for exclusion of children in B group were:

- children with ADHD who also have other chronic conditions that may influence the quality of life (neurosis, anxiety, dissociation, organic diseases);

- the presence of mild, moderate or severe mental deficiency;

- the presence of neurological deficits of language reception;

- lack of compliance.

From all subjects enrolled in the study, urine was collected from the spot (10 mL).

To determine the concentration of cobalt in urine specimens, was used a Varian graphite atomizer coupled with atomic absorption spectrometer system.

Atomic Absorption Spectrometer - AAS 800.

Programmable sample dispenser, standards, modifiers and thinner – PSD.

Water Chiller Model Neslab CFT 33.

Domnick Hunter Nitrogen Generator.

Argon - gas cylinder under pressure purity 99.9999%.

Reagents and equipment specific to a laboratory of analytical toxicology.

To determine the incriminated cobalt in the occurrence of symptoms characteristic of ADHD syndrome, the following methods were used for the analytical toxicology laboratory.

SAMPLE PREPARATION

In 10 ml of urine harvested from each subject in the study lot, 1 ml of 65% HNO₃ was added. The mixture was left in the tube for 20 min and subsequently centrifuged at 2500 rpm for 10 min.

The supernatant was the matrix for analysis on GF-AAS.

OPTOELECTRONIC AAS METHOD FOR ALUMINUM

To determine the concentration of aluminum in the injection matrix, the method used for the GF-AAS Varian system shown in Table 1 and Table 2.

RESULT AND DISCUSSIONS

The average of the urine concentrations of the aluminum was 10.54 µg/L with SD of 9.6 and ASD of 1.42. Sex analysis shows that the average urine concentration in boys was 12.12 µg/L with SD of 9.68 and ASD of 1.98 and in girls, the mean was 8.18 µg/L with SD of 9.26 and ASD of 1.89. The results are shown in Fig. 1. These results show a large distribution of urine concentrations of aluminum. The urinary concentration of aluminum allowance for children is in the range 5 - 30 µg/L³⁵. All children were within the permissible limits of urine concentrations of aluminum. Analysis by Sex shows that the value of urine concentrations of

³⁵ Helmboldt O. Aluminum Compounds, Inorganic. Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH, 2007

aluminum in girls is less than 3.92 $\mu\text{g/L}$ than that of boys. However, the odd Student test shows that the two urinary concentrations of aluminum do not differ significantly statistically for a probability $p > 0.2$. No value of urine concentrations of aluminum exceeds the maximum allowed, which shows that there can be no aluminum contamination of the children in the studied group.

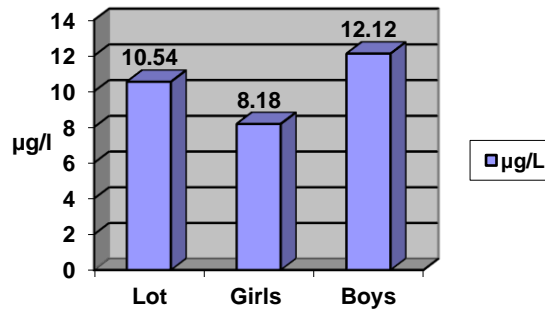


Fig. 1. Distribution of concentrations of aluminum in urine samples.

Within group A, the mean urine concentrations of aluminum were 10.2 $\mu\text{g/L}$ with an SD of 8.27 and an ASD of 1.76. Sex analysis shows that the average urine concentration in boys was 11.16 $\mu\text{g/L}$ with SD of 7.49 and ASD of 2.262 and in girls, the mean was 9.24 $\mu\text{g/L}$ with a SD of 9.25 and a 2.79 ASD. The results are shown in Fig. 2. These results show a large distribution of urine concentrations of aluminum.

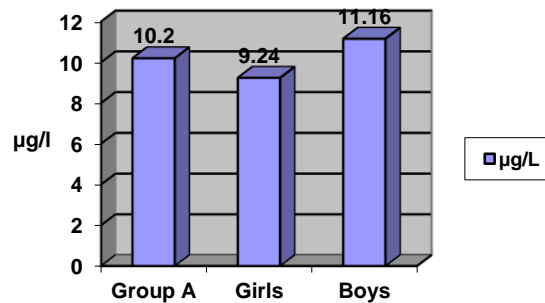


Fig. 2. Distribution of concentrations of aluminum in urine samples of group A.

Sex analysis shows that the value of urine concentrations of aluminum in girls is less than 1.82 $\mu\text{g/L}$ than that of boys. The odd Student Test shows that the two urinary concentrations of aluminum do not differ statistically significantly for a probability $p > 0.6$. Within group B, the mean urine concentrations of aluminum were 10.86 $\mu\text{g/L}$ with an SD of 10.84 and an ASD of 2.21. Sex analysis shows that the average urine concentration in boys was 12.94 $\mu\text{g/L}$ with SD of 11.46 and ASD of 3.18 and in girls, the mean was 8.4 $\mu\text{g/L}$ with SD of 10.02 and ASD of 3.02. The results are shown in Fig. 3. These results show a large distribution of aluminum in urine samples.

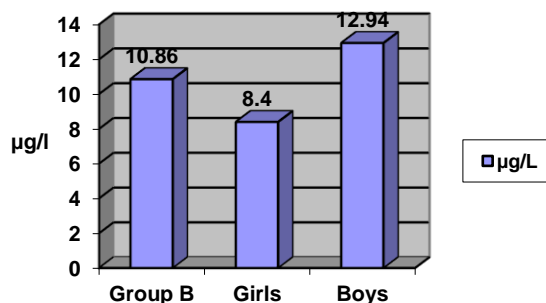


Fig. 3. Distribution of concentrations of aluminum in urine samples of group B.

Analysis by sex shows that the value of urine concentrations of aluminum in girls is less than 4.54 µg/L than that of boys. The odd Student test shows that the two media of urinary concentrations of aluminum do not differ statistically significantly for a probability $p > 0.3$. The difference between the average urinary concentrations of aluminum in the two groups is 0.66 µg/L. Sex analysis shows that the mean aluminum concentration in boys in group B is higher by 1.78 µg/L compared to the average of aluminum urine concentrations in group A boys. The average aluminum concentrations in the A group are higher than the aluminum urine concentrations in the B group with 0.84 µg/L. The results are shown in Fig. 4.

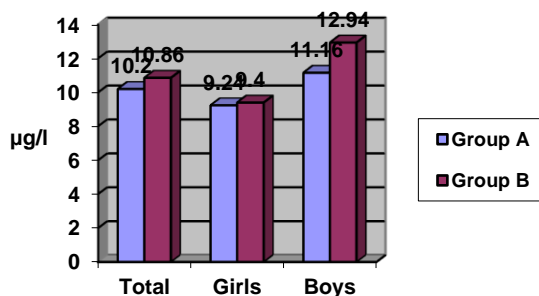


Fig. 4. Distribution of aluminum concentrations of urine samples by groups.

The average of urinary concentrations of aluminum in the two groups do not differ statistically significantly for a probability $p > 0.8$. The difference between the two media is 0.66 µg/L.

The average of urinary concentrations of aluminum in boys in the two groups do not differ statistically significantly for a probability $p > 0.6$. The difference between the two media is 0.78 µg/L.

The average of urinary concentrations of the aluminum of the girls in the two groups do not differ statistically significantly for a probability $p > 0.8$. The difference between the two media is 0.84 µg/L.

CONCLUSIONS

There is no statistically significant difference between the average urine concentrations of the two groups of normal children and the symptoms of ADHD.

It can be argued that the occurrence of symptomatic symptoms characteristic of ADHD can not be correlated with the presence of abnormal values of aluminum in subjects with ADHD.

Analysis of urinary aluminum concentrations in children with ADHD relative to the urinary concentration of these elements in children without ADHD did not reveal any statistically significant difference. These results show that aluminum can not be responsible for the presence of ADHD symptoms.

The developed optoelectronic method is relatively simple, reproducible and has a sensitivity that allows analysis of aluminum concentration in urine samples.

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Table 1. General parameters for AAS.

No.	Parameters	Programming
1.	Type of injection	Auto dilution
2.	Modul de calibrare	Concentrație
3.	Type of measurement	Height peak
4.	Standard replicates	2
5.	Sample replicates	2
6.	Smoothing	9
7.	Wavelength	309.3 nm
8.	Slit width	0.2 nm
9.	Lamp current	10 mA
10.	Background correction	Da
11.	Standard 1	20 µg/l
12.	Standard 2	50 µg/dl
13.	Standard 3	100 µg/dl
14.	Recalibration rate	10
15.	Reslope rate	1
16.	Concentration decimal places	2
17.	Calibration algorithm	New Rational
18.	Replicate % RSD limit	10%
19.	Correlation coefficient limit	0.998
20.	Required detection limit	1 µg/L
21.	Instrument detection limit	0.6 µg/l
22.	Injected volume	15 µl
23.	Sample volume	10 µl
24.	Dilution coefficient	2

Table 2. General parameters for graphite furnace.

PARAMETER	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	STEP 7	STEP 8
Temp. (°C)	40	85	85	95	120	120	1000	1000
Time (s)	2	5	5	40	40	4	6	2
Gases	N	N	N	N	N	Ar	Ar	Ar
Flow (mL/min)	3	3	3	3	3	3	3	0
Read	-	-	-	-	-	-	-	-
Store	-	-	-	-	-	-	-	YES

PARAMETER	STEP 9	STEP 10	STEP 11	STEP 12	STEP 13	STEP 14
Temp. (°C)	2700	2700	3000	3000	40	40
Time (s)	2	1	0.1	2	22.3	3
Gases	Ar	Ar	N	N	N	N
Flow (mL/min)	0	0	3.1	3.1	3	0
Read	YES	YES	-	-	-	-
Store	YES	YES	-	-	-	-

INCISIONAL HERNIA COMPLICATIONS AFTER USING POLIPROPILEN MESH – CASE REPORT

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ABSTRACT:

INCISIONAL HERNIA APPEARS AS A RUPTURE OR A DEFICIENT OF INTERFASCIAL FIBROSIS WHICH HAS A RATE OF 11-23% AFTER A LAPAROTOMY. FOR REDUCING THE RATE OF INCISIONAL HERNIAS PROSTHETIC MESH WERE USED, IN SPECIAL POLIPROPILEN. COMPLICATIONS LIKE SEROMA, FISTULA, BOWEL OBSTRUCTION, CHRONIC PAIN MUST BE CONSIDERED AND AVOIDED. IN CASES OF COMPLICATED INCISIONAL HERNIA WITH LIFE –THREATENING SITUATIONS THE EMERGENCY TREATMENT MUST BE TAKEN. IF THE CORRECT MESH IS NOT USED FOR THE COVER OF AN MINIMAL 5 CM OVERLAP THE POSTOPERATIVE COMPLICATIONS INCREASE DRAMATICALLY. FIBROBLASTS, FOREIGN BODY GIANT CELLS, CAPILLARIES AND MACROPHAGES HAVE DIFFERENT ACTIONS DEPENDING ON THE TOPOGRAPHY AND THE STRUCTURE OF THE MATERIAL USE. MESHES WITH PORE >1000 μM ASSURE A BETTER PROTECTION FROM COLONIZATION OF BACTERIAL DUE LARGE FILAMENTS THAT FACILITATE THE INFILTRATION OF MACROPHAGES. THE SOLUTIONS FOR MESH INFECTION IS THE COMPLETE REMOVAL OF THE PROSTHETIC MATERIAL, A COMPLETE DEBRIDEMENT OF THE REGION AND A CORRECT ADMINISTRATION OF SYSTEMIC ANTIBIOTICS.

KEY WORDS: INCISIONAL HERNIA, COMPLICATIONS, POLIPROPILEN MESH

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INTRODUCTION:

Incisional hernia appears as a rupture or a deficient of interfascial fibrosis.(1) The rate of incisional hernia is situated between 11-23% of laparotomies.(2) Many procedures were describe from beginning, starting with using the nearby structure to different forms of alloplastic meshes. Before the laparoscopy, in which incision length was minimized, all procedures were done throught large incisions.(3) Incisional hernia repair is considered a routine surgery procedure. For reducing the hernia recurrence prosthetic meshes are used in almost half operation performed. (4) Because the prostetin mesh is a foreign material for human tissues, it is also considered the cause of complications like skin infection, fibrosis, seroma, mesh rejection, chronic pain, fistula, bowel obstruction, hernia recurrence.(5). Studies on long-term follow-up complication are limited and only for small groups.(6) When the incisional hernia get complicated, incarcerated or strangulated, site infections can appear and also life-threatening situations.

CASE REPORTS

CASE I



Figure 1. Preoperator view

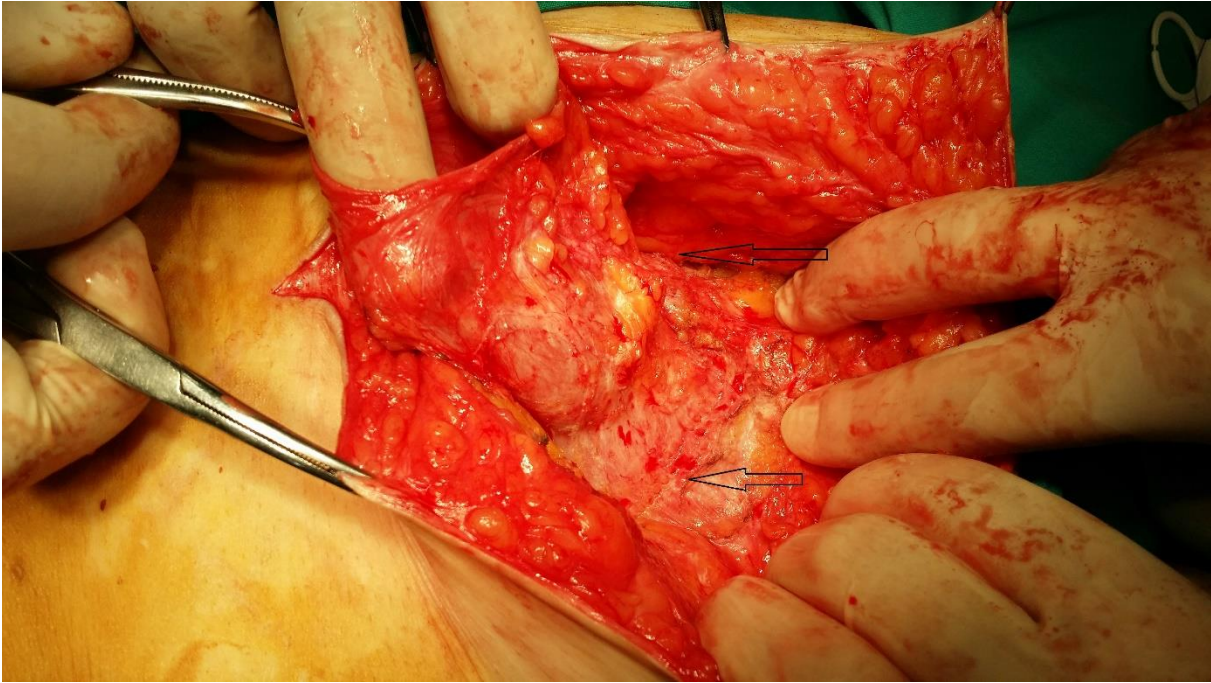


Figure 2. Intraoperator view – upper side of the mesh breach

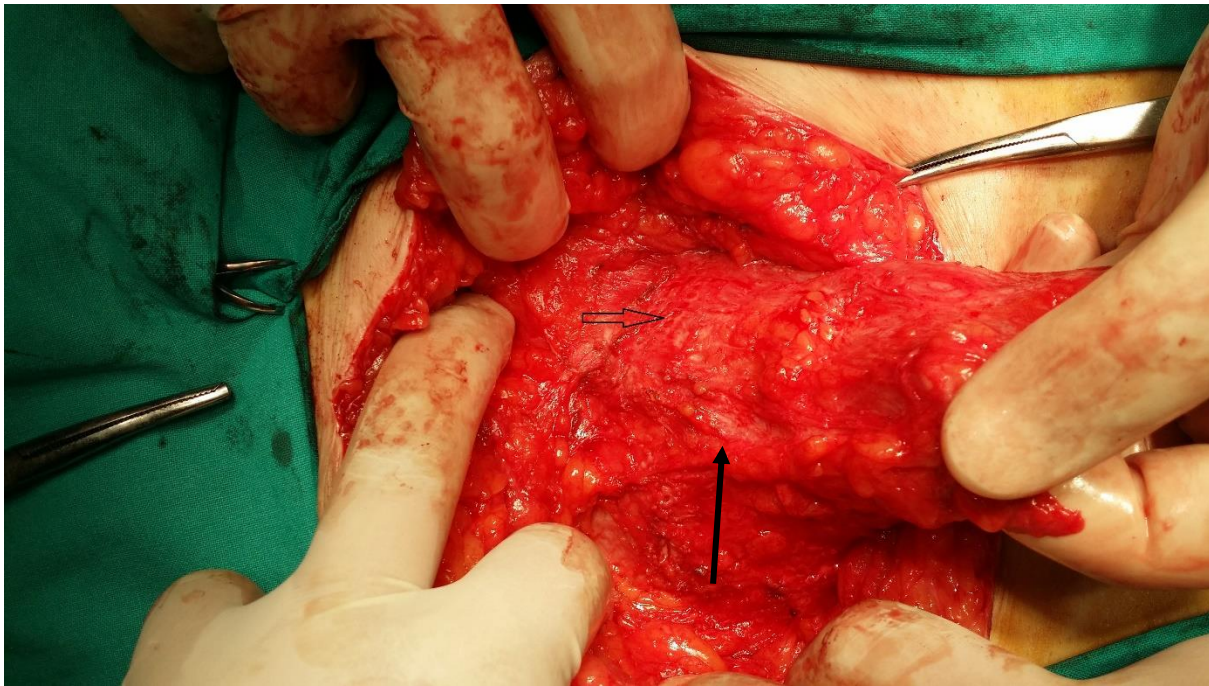


Figure 3. Intraoperator view – image below the mesh breach

A 57 year old woman presented in the Emergency Department with fever, palpable hypogastric mass, intense abdominal pain at the inferior pole of the postoperative scar with a creamy white pus at this level. She observed a bulge at the inferior pole of incision in the last 6 months with progressive grow in the last 3 weeks. Leukocytosis level was 20.000 WBC/mm³ and neutrophilic response, without other abnormality laboratory tests. Abdominal radiography didn't reveal signs of obstruction.

She was first operated 14 years ago when was performed classic cholecystectomy for acute gangrenous cholecistitis.

Two years ago she had 34.5 IMC, chronic obstructive pulmonary disease and a incisional hernia with a length of 10 cm for witch the surgeon used a 20/10 cm polipropilen lightweight mesh – onlay technique without any postoprative complication. She was hospitalized for 7 days.

She was prepare for emergency surgery. Have been taken samples for bacteriological exam from the local fistula. After the dissection of the subcutaneous tissue we found a hole in the middle of the polipropilen mesh with a 5 cm diameter from which a hernia sac prolab. Great omentun and small bowel witout any ischemic or fistulous lesions were reduced in the peritoneal cavity. Parietal defect was closed with PGA No 2 continuous suture. The polipropilene mesh was completely extracted. Two suction drains were positioned in the subcutaneous tissue. There were 7 days of recovery and discharged in good condition.

The antibiotherapy used was Piperacillin-Tazobactam: loading dose of 4.5g in 30 min then 4.5g x 3 per day in 4h infusion. Prolonged injection has been administrated because ensure a superior protection than intermittent injection.

Bacteriological exam reveal that Staphylococcus aureus, Staphylococcus spp. and Streptococcus spp were responsible for local infection.

CASE II

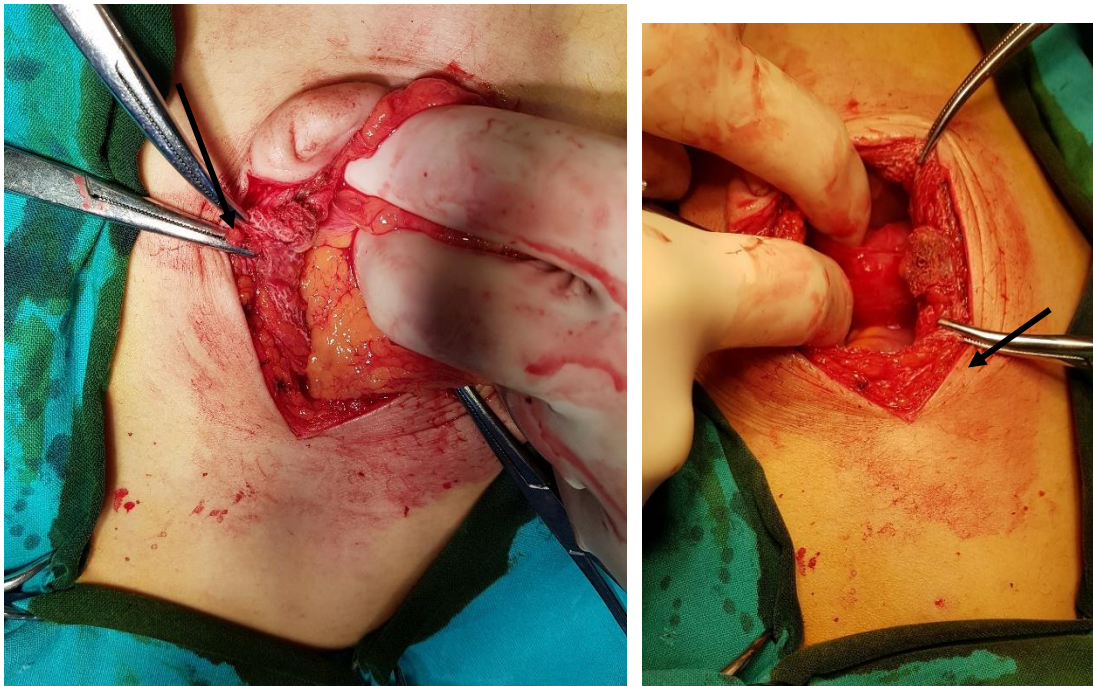


Figure 4 , 5 : Polipropilene mesh agglutinated over the aponeurosis of rectus abdominis

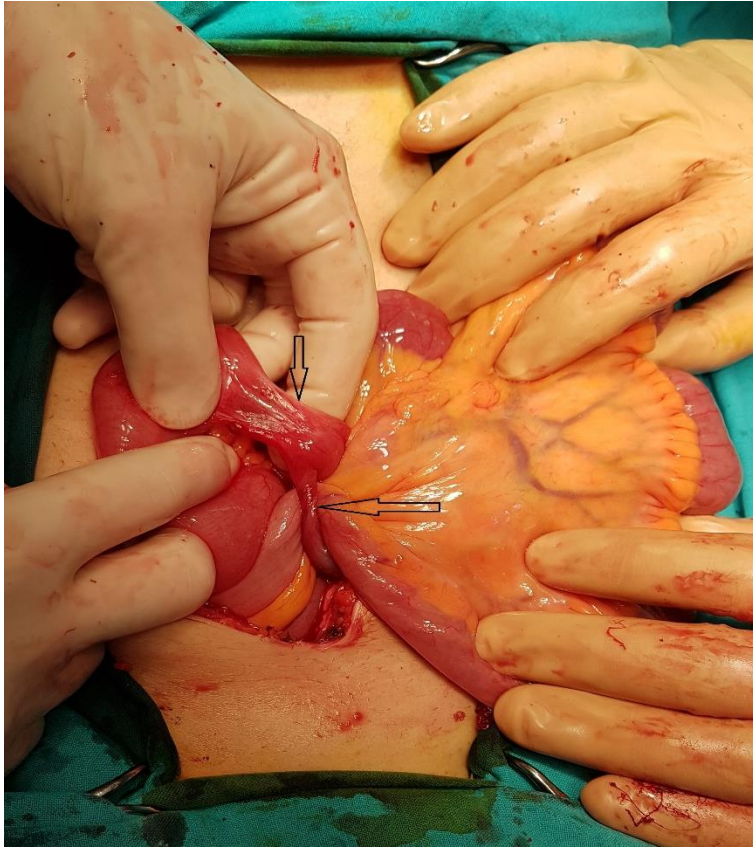


Figure 6: Two site of adhesional small bowel without obstruction

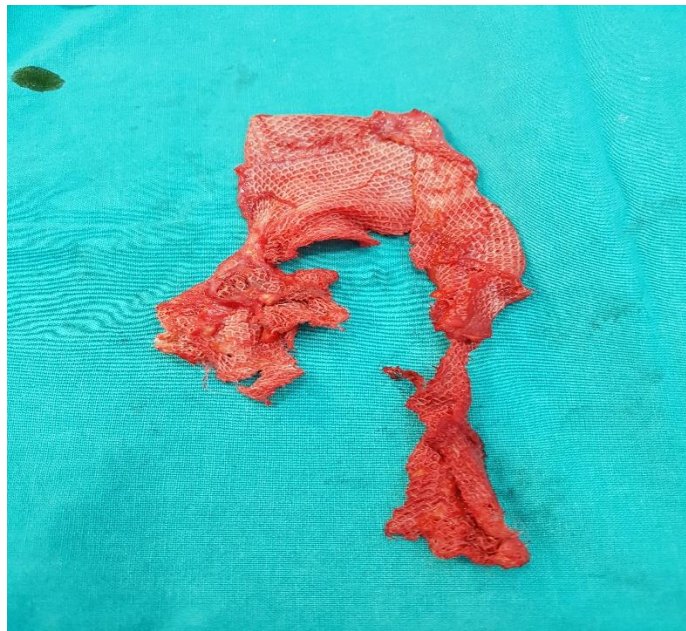


Figure 7: The agglutinated polypropylene mesh

A 49 year old man presented to the Surgery department for abdominal pain, especially at the umbilical level where he noticed a bulge which appeared in the last 3 months, without a progressing growing. His medical history included an umbilical hernia operated 3 years ago – onlay procedure using polypropylene mesh fixed with PGA wires. Laboratory tests were in normal parameters.

At the operation room was performed an iterative longitudinal incision which showed an agglutinated mesh on both sides of the de parietal defect. The polypropylene mesh was extracted. On a 2 cm portion the mesh was in contact with peritoneum and a parietal defect was discovered. Beginning the adhesiolysis were founded two sites where the small bowel was adherent to the mesenter making a loop in which was inserted a part of ileum.

The defect was closed with PGA No 2 continuous suture and was applied an ultralight polypropylene mesh fixed with 3/0 Polypropylene wires. One suction drain was positioned in the subcutaneous tissue. The patient was discharged after 3 days in good conditions.

Follow-up at one year showed a plain operation zone, without any mass or modified regional skin.

DISCUSSION:

Theodor Billroth, in 1890, came with the assumption that the best way to repair a hernia is to use a prosthetic material. Many materials used on hernia repair generated rejections, infections and recurrences. (2,12,13)

Incisional hernia is generated by different factors depending on the patient but also on the doctor (obesity, cardiac and pulmonary problems, sepsis, types of wires used for suture, the surgeon techniques). (1,5,6)

The recurrence for incisional hernia is 4.8% smaller in mesh usage. In a 5 years period 1.4% of cases in which was used polypropylene mesh were reoperated for enterocutaneous fistula, bleeding or bowel occlusion.(7). One randomized clinical trial and few small retrospective studies debate the complication generated by polypropylene mesh. (6, 8,9)

If the correct mesh is not used for the cover of an minimal 5 cm overlap the postoperative complications increase dramatically.(10,11) Lower inflammation near the mesh site reduces long-term complications despite the intense fibrosis that anchor the prosthesis in the correct tissue. Fibroblasts, foreign body giant cells, capillaries and macrophages have different actions depending on the topography and the structure of the material used. Meshes with pore >1000 µm assure a better protection from colonization of bacteria because of large filaments that facilitate the infiltration of macrophages.(14,15).

Incisional hernia complications may be preventable by using strict rules of antisepsis, rigorous hemostasis and also correct tissue handling. Using systemic antibiotics preoperative or postoperative, collagen tampons or releasing gentamicin collagen did not show a general solution. (16,17,18,19) “Empirical antibiotic therapy protocols for community- must be established on the basis of regular analysis of national and regional microbiological data in order to quantify and monitor the course of microbial resistance in the community.” (20)

CONCLUSIONS:

For open surgery, mesh infections are a real concern despite the correct choice of prosthetic material, the rigorous sterility and proper antibiotic coverage. Using the correct mesh and the wires for proper suture assure a low rate of mesh-related complication.

The solutions for mesh infection is the complete removal of the prosthetic material, a complete debridement of the region and a correct administration of systemic antibiotics.

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