



## EPIDEMIOLOGICAL AND PATHOHISTOLOGICAL CHARACTERISTICS OF TESTICULAR NEOPLASMS IN THE ZENICA-DOBOJ CANTON, BOSNIA AND HERZEGOVINA: A THREE-YEAR MONOCENTRIC STUDY

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### Summary

*Aim:* The primary aim of the study was to determine the incidence of testicular neoplasms in the Zenica-Doboj Canton (ZDC) region for the period from 2019 to 2021. Also, the study aimed to examine the age structure of the affected population, the frequency of testicular neoplasms in all the ZDC cities and municipalities, and the pathohistological characteristics of neoplasms.

*Material and methods:* The study was conducted at the Oncology and Radiotherapy Department of the Zenica Cantonal Hospital. The study period refers to the time interval from January 2019 to December 2021. The study included 37 patients with a verified diagnosis of testicular neoplasm.

*Results:* Arithmetic mean of patients' age was 33.49 years, while the standard deviation was 12.59. Most respondents, accounting for 40.5%, were aged 26-35 years. The incidence of testicular neoplasms in the ZDC region was 4.2/100,000 persons in 2019, 3.08/100,000 persons in 2020, and 3.10/100,000 persons in 2021. Most diagnosed neoplasms (48.6%) were the myxoid type germ cell originating tumors.

*Conclusion:* The incidence of testicular neoplasms in the ZDC was 4.2/100,000 persons in 2019, 3.08/100,000 persons in 2020, and 3.10/100,000 persons in 2021.

KEYWORDS: *testis, neoplasm, Bosnia and Herzegovina*

### INTRODUCTION

Testicular neoplasms account for 1% of malignant tumors; however, they are the most common solid tumors in men aged between 15 and 35(1). There is a peak in incidence of these tumors in men aged 60 and over, with seminomas as the most common histological type of testicular tumor(1). The incidence of testicular tumors has increased

significantly over the past four decades(2). Testicular neoplasms are divided into major pathohistological categories: germ cell tumors and tumors of specialized stromal cells (Leydig and Sertoli cells)

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(3). Tumors of the germinal epithelium make up 95% of testicular tumors, and the remaining 5% are stromal tumors. Testicular tumors also include much rarer metastatic tumors(3).

There is a notable scarcity of available literature addressing the incidence of testicular neoplasms, referring specifically to Bosnia and Herzegovina (B&H). This gap in research can be attributed to the absence of a unified national registry for testicular neoplasms in the country. Consequently, data collection is reliant on information gathered from individual healthcare institutions where patients seek treatment. Such scarcity underscores the necessity for localized studies to provide a comprehensive understanding of the prevalence and characteristics of testicular neoplasms in this region.

The primary aim of this study was to establish the incidence of testicular neoplasms in the ZDC over a three-year period spanning from 2019 to 2021. In addition to this overarching objective, the study sought to analyze the age distribution of affected individuals, evaluate the frequency of testicular neoplasms across all cities and municipalities within the ZDC, and delve into the pathohistological characteristics of the identified neoplasms. This comprehensive approach aimed to fill the existing research gap and provide valuable insight into the specific epidemiological profile of testicular neoplasms in this region of B&H.

## MATERIAL AND METHODS

The study was conducted at the reference center for ZDC, the Department of Oncology and Radiotherapy of the Zenica Cantonal Hospital. The study period refers to the time interval from January 2019 to and including December 2021. The criteria for inclusion in the study were: a) that the patient has a registered residence in the ZDC region, that is, that the patient is a citizen of one of the municipalities or cities in the canton; and b) that the patient has a confirmed pathohistological diagnosis of testicular neoplasm. All testicular neoplasms were confirmed by the Pathology Department of the Zenica Cantonal Hospital.

Data on all patients was processed using Microsoft Excel. Variables were created using data on age, pathohistological type, the presence of metastases, and the presence of lymphovascular

invasion (LVI). The incidence of testicular neoplasms was determined for the ZDC and its municipalities and cities, i.e.: Breza, Doboj Jug, Kakanj, Maglaj, Olovo, Tešanj, Vareš, Visoko, Zavidovići, Zenica, Žepče and Usora. Population data was obtained from the Federal Agency for Statistics of Bosnia and Herzegovina. In 2019, the total population of the ZDC was 358,292 persons. This number decreased to 357,275 in 2020, and 354,285 in 2021. The incidence of testicular neoplasms is reported per 100,000 persons. The Age-Standardized Incidence Rate (ASIR) is obtained by multiplying the ratio of the total population ( $N$ ) to the population in a specific age group ( $N_i$ ) by the ratio of the standard population in that age group ( $N_{std,i}$ ) to the total standard population ( $N_{std}$ ) and scaling with 100,000 for standardization. The data was processed using the Statistical Package for the Social Sciences software (SPSS, version 26.0). For the purposes of this study, descriptive statistics, determination of frequency and percentage, and the  $\chi^2$  test were used to test for statistically significant differences in the examined sample. The level of significance was set at  $< 0.05$ .

## RESULTS

The youngest patient in the ZDC who was diagnosed with testicular neoplasm was 18 and the oldest 85 years old. The arithmetic mean of the patients' age was 33.49 years (table 1). The majority of patients (40.5%) were in 26-35 and 27% in 16-25 age group. The third most common age group was 36-45 years. There were no diagnoses in the 0-15 age group, while the other age groups were evenly represented (2.7%) (Figure 1).

The highest number of patients was diagnosed in 2019 ( $n = 15$ ), followed by fewer cases in

Table 1.

*Age characteristics of the respondents*

Variable	N	%	Min	Max	Mean	SD	
Age	0-15	0					
	16-25	10					
	26-35	15					
	36-45	9	24.3	18	85	33.49	12.59
	46-55	1	2.7				
	56-65	1	2.7				
	above 65	1	2.7				
Total	37	100.0					

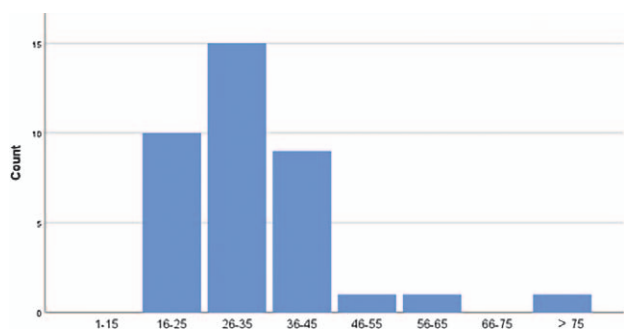


Figure 1. Age distribution of patients

2020 and 2021 (n = 11). There were no statistically significant differences observed in 2020 (p = 0.174) and 2021 (p = 0.062). The trend from 2019 continued in 2020, with the most cases verified in Zenica. In 2021, the highest number of cases was established in Kakanj (45.45%). The highest incidence was recorded in Kakanj in 2021, with 0.0136% of persons diagnosed (13.6/100,000). A significantly high incidence of 0.046 patients (4.57/100,000) was also recorded in Tešanj in 2019 (table 2).

Table 2.

Incidence per 100,000 persons in the ZDC municipalities

Municipality	Incidence (n/100,000)		
	2019	2020	2021
Breza	0.000	0.000	0.000
Doboj-Jug	0.000	0.000	0.000
Zenica	7.318	5.500	1.847
Kakanj	2.697	2.701	13.617
Maglaj	0.000	0.000	0.000
Olovo	0.000	0.000	0.000
Tešanj	4.567	0.000	0.000
Usora	0.000	15.775	0.000
Vareš	12.731	12.948	0.000
Visoko	7.645	2.558	2.586
Zavidovići	0.000	2.856	5.761
Žepče	0.000	0.000	3.377
$\chi^2$	15.000	12.500	15.000
df	5	6	5
<b>p</b>	<b>0.010</b>	<b>0.052</b>	<b>0.010</b>

Additionally, a notably high incidence of 7.31 cases per 100,000 persons was observed in Zenica in 2019. However, the incidence decreased significantly to 1.85/100,000 in 2021 (table 2). Vareš also recorded a significant incidence of approximately 13 cases per 100,000 persons in 2019 and 2020. A statistically significant difference in incidences be-

tween the observed municipalities and cities was determined for 2019 (p = 0.010) and 2021 (p = 0.010). Taking into account variations in population size in municipalities and cities, the most accurate indicator is the canton-wide incidence, as presented in table 3. The overall incidence rate of the variable decreased from 4.19 cases per 100,000 persons in 2019 to 3.08 cases per 100,000 persons in 2020, with a slight increase to 3.10 cases per 100,000 persons in 2021. Within the 16-64 age group the incidence rates mirrored the overall trend, while in >65 age group the number of cases reported in 2019 was minimal, and no cases were reported in 2020 and 2021.

Table 3.

Incidence for the canton from 2019 to 2021 with age-specific rate

Variable/Year	2019	2020	2021
Incidence (n/100,000)	4.19	3.08	3.10
Age-specific incidence rate			
16-64 (n/100,000)	3.90	3.08	3.10
>65 (n/100,000)	0.29	0	0

The most frequently diagnosed neoplasms were of the myxoid type originating from germ cells (48.6%). Testicular seminomas accounted for a significant share (35.1%). Embryonic testicular carcinomas (5.4%) and teratocarcinomas (2.7%) had lower representation percentages (table 4). Pathohistological verification was not possible or refused by three patients. A statistically significant difference (p < 0.001) was confirmed in the pathohistological forms of neoplasms in the respondents. Metastatic processes caused by the primary testicular neoplasm were equally verified in 45.9% of cases and metastasis-free cases. A statistically significant difference in metastasis distribution was confirmed (p = 0.005). LVI was present in 51.3% of respondents, with statistically significant differences evident (p < 0.001).

## DISCUSSION

The total number of patients diagnosed with testicular cancer in the ZDC region in the three-year period, from 2019 to 2021, was 37. The arithmetic mean of patients' age in the examined sample was 33.49. According to Gajendran et al.(4), Yamashita et al.(5) and Secondino(6), testicular

Table 4.

## Pathohistological characteristics of tumors

Variables		n (%)	$\chi^2$	df	<i>p</i>
PHD	Carcinoma embionale testis	2 (5.4)	44.892	5	<b>&lt;0.001</b>
	Tumor mixtus cellurarum germinativum	18 (48.6)			
	Seminoma testis	13 (35.1)			
	Teratocarcinoma testis	1 (2.7)			
	Unknown	3 (8.1)			
Metastases	Yes	17 (45.9)	10.595	2	<b>0.005</b>
	No	17 (45.9)			
	Unidentified	3 (8.1)			
Lymphovascular invasion	Yes	19 (51.3)	36.784	5	<b>&lt;0.001</b>
	No	12 (32.2)			
	Unidentified	6 (16.2)			
Total		37 (100)			

cancer is the most commonly diagnosed in men aged between 22 and 35. Abomelha(8) found the average age of patients with testicular neoplasm diagnosis in a twenty-year sample in Saudi Arabia to be 34.5 years. Generally, testicular cancer appears in the adolescent and early adult period, which was also confirmed in the ZDC. The National Cancer Institute of the United States of America reports that the incidence of testicular cancer is low in men older than 50, which is consistent with the results of this study. According to previous studies, there has been a noticeable increase in arithmetic mean of the age of respondents in whom the presence of testicular cancer, especially testicular seminoma, was verified (5,9,10).

Testicular cancer is more prevalent in developed than in developing countries. Although higher rates are observed in white men, the incidence of testicular cancer among non-white and immigrant populations in the United States is rising, for reasons that remain unclear(11). Additionally, synchronous contralateral tumors are detected in 0.6% of cases, while metachronous contralateral tumors are observed in 1.9% of cases(12).

According to predictions, increase in testicular cancer by 2025 could be 25% higher compared to 2005(13), which is a fact to worry about. The incidence in Western countries ranges from 3 to 11 cases per 100,000 persons. The highest incidence was recorded in Norway, Slovenia and Denmark(14). In this particular sample, the highest incidence was recorded in 2019, with a verified testicular neoplasm of 4.19 cases per 100,000 per-

sons. A lower incidence was recorded in 2020 (3.08/100,000) and 2021 (3.10/100,000). In North America, the incidence was 5.9 cases per 100,000 persons in 2019, and it was significantly higher in whites (8.3) than in blacks (2.3). In South America, Argentina has the highest incidence, with 8.7 cases per 100,000 persons. In Europe, 25,058 new cases of testicular cancer were registered in 2020, which accounts for about 34% of the total number of diagnosed testicular cancers worldwide(14). The highest incidence was recorded in Norway, with 11.8 cases per 100,000 persons. Slovenia has the second highest incidence with 10.8 cases per 100,000 persons, and Denmark has the third highest incidence with 10.4 cases per 100,000 persons. Of particular concern is the fact that Slovenia has almost doubled the incidence of testicular cancer in the past eighteen years(14). Germany also has a high incidence, with 10 cases per 100,000 persons, as well as Switzerland (9.4/100,000) and France (9.0/100,000).

When it comes to Middle East, Turkey has the highest incidence of 4 cases per 100,000 persons, which is close to the results of the ZDC sample(14). A lower incidence is observed in Japan (2.9/100,000) and China (1.6/100,000).

African countries have the lowest incidence, ranging from 0.3 to 0.6 cases per 100,000 persons, but it is necessary to underline the unreliability of this information due to the lack of record keeping and poor diagnostic activities(15).

The most common non-seminoma testicular neoplasm is myxoid germ cell tumor according to Chakrabarti et al.(16), which is in agreement with



the situation in the ZDC region. Namely, 48.6% of respondents had a verified myxoid germ cell tumor. Testicular germ cell tumors are the most common testicular neoplasms(17). No tumor neoplasm of germ cell origin was verified. LVI was verified in 51.3% of respondents, which is significantly more than the presence of LVI (26%) in the study by Yossepowitch et al.(18). According to French et al.(19), 30% of the examined sample had LVI. Almost half of the patients had metastases (45.45%), which corresponds to the results of a meta-analytic study Block et al.(20).

## CONCLUSION

In conclusion, this study provides valuable insight into the incidence and characteristics of testicular cancer in the ZDC region over a three-year period. The findings align with global trends, indicating a higher prevalence in developed countries, and a typical age range of diagnosed persons being young adults. The observed increase in cases of testicular seminoma among older respondents is noteworthy. The prevalence of myxoid germ cell tumors and the high occurrence of LVI underscore the importance of strategies relying on accurate diagnostic methods and treatment strategies. Future research and initiatives shall certainly address the evolving landscape of testicular cancer.

One limitation of this study is its exclusive focus on the ZDC region, potentially not capturing the comprehensive demographic and environmental determinants impacting testicular cancer incidence. Additionally, the categorization of residents into three groups by the official statistical agency posed a constraint in calculating ASIR.

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#### Sažetak

### EPIDEMIOLOŠKE I PATOHISTOLOŠKE KARAKTERISTIKE NEOPLAZMI TESTISA U ZENIČKO-DOBOJSKOM KANTONU, BOSNA I HERCEGOVINA: TROGODIŠNJA MONOCENTRIČNA STUDIJA

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**Cilj:** Osnovni cilj istraživanja je utvrditi incidenciju neoplazmi testisa na području Zeničko-dobojskog kantona za razdoblje od 2019. do 2021. godine. Također, cilj je bio ispitati dobnu strukturu oboljele populacije, učestalost neoplazme testisa u svim gradovima Zeničko-dobojskog kantona, te patohistološke karakteristike neoplazmi.

**Materijal i metode:** Istraživanje je provedeno na Odjelu za onkologiju i radioterapiju Kantonalne bolnice Zenica. Razdoblje pregleda odnosi se na vremenski interval od siječnja 2019. do prosinca 2021. Istraživanjem je obuhvaćeno 37 ispitanika s verificiranom dijagnozom neoplazme testisa.

**Rezultati:** Aritmetička sredina bolesničkih godina bila je 33,49, a standardna devijacija 12,59. Najveći broj ispitanika pripada dobnoj kategoriji od 26-35 godina, u postotku od 40,5%. Učestalost novotvorina testisa na području Zeničko-dobojskog kantona za 2019. godinu iznosila je 4,2/100.000 stanovnika, za 2020. godinu 3,08/100.000 stanovnika, a za 2021. godinu 3,10/100.000 stanovnika. Većina dijagnosticiranih novotvorina bila je miksoidnog tipa, podrijetlom iz spolnih stanica (48,6%).

**Zaključak:** Učestalost novotvorina testisa na području Zeničko-dobojskog kantona u 2019. godini iznosila je 4,2/100.000 stanovnika, u 2020. godini 3,08/100.000 stanovnika, a u 2021. godini 3,10/100.000 stanovnika.

**KLJUČNE RIJEČI:** *testis, neoplazma, Bosna i Hercegovina*