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**Prevalence and characteristics of hepatic hemangiomas assessed by  
ultrasound – a single-center experience**

Учесталост и карактеристике хемангиома јетре дијагностикованих  
ултразвуком – искуство једног центра

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## Prevalence and characteristics of hepatic hemangiomas assessed by ultrasound – a single-center experience

### Учесталост и карактеристике хемангиома јетре дијагностикованих ултразвуком – искуство једног центра

#### SUMMARY

**Introduction/Objective** Liver hemangioma is the most common benign tumor of the liver, with estimated prevalence of 2.5-4%. This study aimed to investigate the prevalence and clinical characteristics of hepatic hemangioma in one Primary Care Center in Serbia.

**Methods** We conducted a cross-sectional study, which included patients examined in Primary Care Center "Dr Simo Milošević" in Belgrade, Serbia (December 2017 - March 2020). Patients with suspected atypical changes, malignancies, viral hepatitis infections, and liver cirrhosis were excluded from the study.

**Results** A total of 567 patients were included in this study (men 42.5%). In 27 patients (4.76%) a diagnosed of hemangioma was made (male:female ratio: 1.1:1). The total number of hemangiomas detected was 48. Hemangiomas were most commonly found in the right liver lobe (32/48, 66.7%). In this study, hemangiomas were most commonly localized in the fourth liver segment (11/48, 22.9%). The mean diameter of the hemangioma was 13.8 mm. In the half of patients diagnosed with hemangioma, more than one hemangioma was detected (13/27, 48.1%).

**Conclusion** Hemangiomas of the liver are commonly multiple. No sex difference in hemangioma prevalence was noted. The right liver lobe is the most common hemangioma localization in this study cohort.

**Keywords:** liver hemangioma; ultrasonography; frequency

#### САЖЕТАК

**Увод/Циљ** Хемангиоми су најчешћи бенигни тумор јетре са процењеном учесталошћу од 2,5-4%. Ова студија је имала за циљ да истражи преваленцу и клиничке карактеристике хемангиома на основу ултразвучног преглед абдомена у једном дому здравља у Србији.

**Метод** Ради се о студији пресека у којој су укључени пацијенти прегледани у Дому здравља "Др Симо Милошевић" у Београду, Србији, за период децембар 2017. – март 2020. године. Пацијенти са суспектним атипичним променама, малигнитетима, вирусним хепатитисима и цирозом јетре нису укључивани у студију.

**Резултати** Студија обухвата укупно 567 пацијената (мушкарци 42,5%). Код 27 пацијената (4,76%) дијагностиковани су хемангиоми (однос мушкарци:жене 1,1:1). Укупно је дијагностиковано 48 хемангиома. Најчешћа локализација хемангиома (32/48, 66,7%) била је у десном режњу јетре. Гледајући по сегментима, хемангиоми су најчешће били локализовани у четвртог сегменту (11/48, 22,9%). Просечна величина хемангиома била је 13,8 мм. Скоро половина пацијената са дијагностикованим хемангиомом имала је више од једног хемангиома (13/27, 48,1%).

**Закључак** Хемангиоми јетре углавном нису појединачни. Није показана разлика у учесталости међу половима. Десни режањ јетре је био најчешћа локализација хемангиома у нашој студији.

**Кључне речи:** хемангиоми јетре; ултразвук; учесталост

## INTRODUCTION

The liver hemangioma is the most common benign tumor of the liver [1, 2]. Hemangiomas are the third most common liver lesion with a frequency of 3.6%, after focal fatty sparing of the liver with prevalence of 6.3% and liver cysts with prevalence of 5.8% [3]. The number of hemangiomas in patients has increased in recent years, most likely due to the increased number of medical examinations. Its incidence ranges from 2.5-4% in ultrasound series.

In most studies hemangiomas were more frequent in female than in men, with ratio of 5:1 to 1.9:1. Hemangiomas were most common in patients between 30 and 60 years old [4–9].

There are three types of liver hemangioma: cavernous, capillary and anastomosing hemangiomas. The most frequent is cavernous hemangioma [10]. Ultrasound has proven to be a sovereign method for diagnosing hepatic hemangiomas with an assessment of sensitivity of 96.9% and specificity of 60.3% [11]. Most of the patients with liver hemangioma have no symptoms. Treatment is not necessary if the tumor is asymptomatic and patients are only followed up [12]. If the tumor size increases, it can cause symptoms such as abdominal discomfort, pain, distension, vomiting, poor appetite, pressure on the local structures and even serious complications such as tumor rupture or bleeding [13]. In that case, the surgery is a choice of treatment [14, 15, 16].

To date, there are lack of epidemiological data on the frequency of liver hemangiomas in our region. There are only few available studies done in Germany, Italy, Iran, China and Chile [3, 4, 6, 9, 17].

This study is aim to investigate the prevalence and clinical characteristics of hepatic hemangioma in one Primary Care Center in Serbia. According to our knowledge studies like this have not previously been conducted in this field in our region.

## METHODS

Data for this cross-sectional study were collected during regular ultrasound examinations in Primary Care Center "Dr Simo Milošević", Belgrade, Serbia, the period from December 2017 to March 2020. Data were collected from a review database of two physicians who performed the real-time gray-scale sonography.

The study population includes patients older than 18 years old who underwent an abdominal ultrasound. Patients were referred for an ultrasound examination by a general practitioner as part of regular medical check-ups or because of abdominal pain, abdominal discomfort and due to regular control of the underlying disease. Patients with suspected atypical changes, malignancies, viral hepatitis infections and liver cirrhosis who were diagnosed with liver lesions were excluded from the study.

During the examination, in addition to the basic abdominal ultrasound data, data on the size, location and number of liver hemangiomas were also recored. The diagnosis of the hepatic hemangioma was determined using ultrasound parameters which include homogenous hyperechoic mass with acoustic enhancement, sharp margins and absence of halo sign [18]

(Figure 1). Each case that was not typical was sent for further diagnosis and was excluded from the study.

The examination was done on SIEMENS ACUSON NX3 Elite and TOSHIBA Xario 100 xario devices.

The study is conducted in accordance with Good Clinical Practice guidelines (ICH-GCP), the Declaration of Helsinki and applicable local regulations. The study protocol was approved by the Institutional Ethics Review Board of the Dr. Simo Milošević Primary Care Center, Belgrade, Serbia. Patient consent was waived due to the retrospective nature of the study.

### Statistical analysis

All collected data were statistically processed in SPSS 20.0 statistical software (IBM corp.). For continuous variables, the mean and standard deviation were calculated, while categorical attributes were presented in absolute and relative frequencies. The Mann-Whitney U test was used to compare the mean size. Corrected p values < 0.05 were considered statistically significant.

## RESULTS

In this study 567 patients met the criteria for inclusion, of whom 326 female (57.5%), and 241 were men (42.5%). The mean age of patients was  $61 \pm 13$  years. The number of patients diagnosed with hemangiomas was 27 (4.76%). Among patients with diagnosed hemangiomas, a total number of 48 individual hemangiomas were found. Out of this number, 13 (48.1%) patients were female and 14 (51.9%) were male, with a ratio of 1:1.1. Descriptive clinical characteristics of the group are described in Table 1.

The mean age of patients diagnosed with hemangiomas was  $57 \pm 13$  years old (range 30-88 years). Hemangiomas were most commonly diagnosed in patients aged 60-69 years (11, 40.7%). The distribution of other age groups with decreasing frequency was as follows: 50-59 years (7, 25.9%), 40-49 years (4, 14.8%), 30-39 years (3, 11.1%), 80-89 years (2, 7.4%).

The mean size of the hemangioma was  $13.8 \pm 8.2$  mm. The largest hemangioma was 42 mm in diameter and the smallest one was 5 mm in diameter. There is no statistically significant difference between men and female in the mean values of hemangioma size ( $p > 0.05$ ). The size of the hemangioma was missing in two patients. Only one hemangioma was larger than 40 mm

which classifies as the giant hemangioma. The distribution of hemangiomas according to their diameter is presented in detail in Table 2.

The most common hemangioma localization was the right liver lobe (n = 32, 66.7 %). The distribution of hemangiomas by segments is presented in Figure 2.

Thirteen (48.1%) patients had two or more hemangiomas (9 male, 4 female). Out of 27 patients diagnosed with hemangioma, 8 (29.62%) of them had previously known to have the liver hemangioma. Data were not available regarding the method used for the initial diagnosis. Patients were instructed and advised to have a follow-up visit in one year (n = 4, 14.81%), or were referred to the hepatologist for a further diagnostic work-up (n = 7, 25.92%). Data regarding the follow-up plan was not available for the remaining patients (n = 8, 29.62%).

## DISCUSSION

Cavernous hemangioma accounts for 55 % of all benign liver tumors [1]. The most common symptoms associated with hepatic hemangioma are abdominal pain and discomfort [5]. There is limited data on the incidence of liver hemangiomas in the general population diagnosed by ultrasound. Our results indicate that the frequency of hemangiomas in our center diagnosed by ultrasound is 4.76%. This frequency is similar as in previous published studies from Germany, Italy and Iran performed using ultrasound [3, 6, 9]. In a large retrospective cross-sectional study conducted by Mocchegiani F et al., the incidence of diagnosed hemangiomas was 2.5% in a population of 83,181 patients undergoing computed tomography (CT) and magnetic resonance imaging (MRI) [9]. In the study done by Horta G. and colleagues, among 1184 patients, 61 (5%) were found to have a hemangioma detected by CT [17]. A liver hemangiomas were identified by ultrasound in 1640 of 45319 patients (3.3%) in a German study [3]. The study by H. Yongfei et al. indicates that the frequency of hepatic hemangioma in a population of 246 149 examined patients is 1.2% [19].

In our study, hemangiomas were found to be similar between men and female, with the ratio of men to female 1.1:1. Our study and a couple of previous studies indicate that hemangiomas are not more common in the female population as previously thought and that their prevalence is almost equal in both sexes [3, 9, 20]. According to Mocchegiani F et al., the prevalence of liver hemangiomas is 47.7% in female and 52.3% in men [9]. Men's frequency in the study by Liu X and colleagues is 3.36%, while women's frequency is 2.89% [20]. In the large study by Kaltenbach TE et al., the gender distribution of hemangioma was nearly balanced, with 53.4%

female and 46.6% males [3]. This is most likely due to an increase in the number of males who get regular medical check-ups, as well as larger studies in this field.

The real number of hemangiomas in our population is presumably higher, because all atypical lesions were excluded from the study and sent for further diagnostics. In our study, the average age was 57 years old, hemangiomas were most often diagnosed in the group of patients aged 50-69, which is a slightly older group compared to previous studies. Recent data by Liu X. et al showed that hemangiomas were most often diagnosed in the group of patients aged 40-49 [20]. Also, in the study by Huang J. et al. hemangiomas were most often diagnosed in the group of patients aged 41-60 years [21].

The most intensive growth of hemangiomas was observed in 30-39 years old, while after the age of 50 there is almost no increase [20]. In the multicentric study done by Tang T et al., 25% of hemangioma patients underwent treatment as a result of progressive hemangioma enlargement [4]. Progressive growth of hemangiomas is considered to be more than 2 cm per year.

In our study, hemangiomas were most commonly diagnosed in the right liver lobe with percentage of 66.7%, which is consistent with findings in the previous studies [6]. Recent data by Yoon SS et al. the frequency of hemangioma in the right lobe is 58% [5]. In the study by H. Yongfei et al., the most common localization was also in the right lobe with a frequency of 80.3% [19]. In our study, the fourth liver segment was the most common localization (22.9%).

The most common hemangioma diameter ranged from 10 to 19 mm. When a hemangioma is larger than 4cm in diameter, it is referred to as a giant hemangioma [10]. Only one of our patients had a diameter of hemangioma over 40 mm (42mm). The mean diameter of the hemangiomas was 13.8 mm and there was no statistically significant difference between the genders.

It was noticed that a large number of patients (48.1%) had two or more hemangiomas, and that it was more common in men than in female. Yoon SS et al. found that 49% of patients had more than one liver hemangioma [5]. This data suggests that if a hemangioma is diagnosed, the patient is quite likely to have more than one hemangioma.

By searching the available literature, there is no evidence for malignant transformation of liver hemangiomas. A case of cholangiocarcinoma growing within a giant hemangioma was described, but without proven malignant hemangioma transformation [22]. The differential diagnosis presents the biggest challenge to hepatic hemangioma diagnosis. Many primary tumors of the liver and secondary metastases can be differentially challenging [23]. If the

hemangiomas are smaller, they may be completely fibrosed and mimicking the diagnosis of a malignant disease [24, 25].

There are a few limitations of the study. First, this is a single-center retrospective study and there was a small sample size. Second, there was lack of follow-up for patients diagnosed with hemangiomas or other atypical lesions.

## CONCLUSION

This is a unique study on the frequency of hemangiomas in one Primary Care Center in Serbia. Because the patients do not fall under any specific disease categories, we can consider them as a cohort of the general population, which gives credibility to these results. Certain characteristics and specifics of our population could point out some characteristics of hemangiomas that would help doctors in more accurate diagnosis and further follow-up of these patients.

In our patients' cohort, hemangiomas were commonly multiple, and most commonly localized in the fourth liver segment. We did not detect any difference in hemangioma prevalence between the sexes. Patients who have discomfort or hemangiomas that grow more than 2 cm per year should consider further evaluation and surgical treatment. Hemangiomas with an uncharacteristic appearance on ultrasound should be referred for further diagnostics, primarily by MRI and CT.

**Data availability statement:** Data used in this research are available from the corresponding author (T.M.) upon reasonable request.

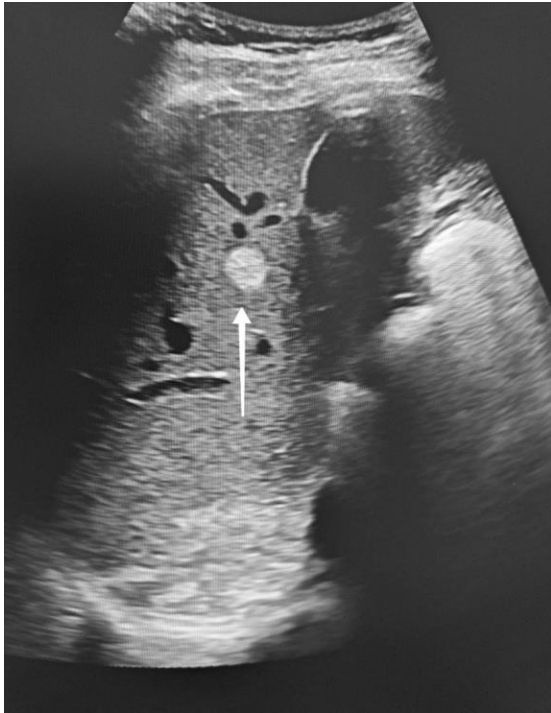
**Conflicts of interest:** None declared.

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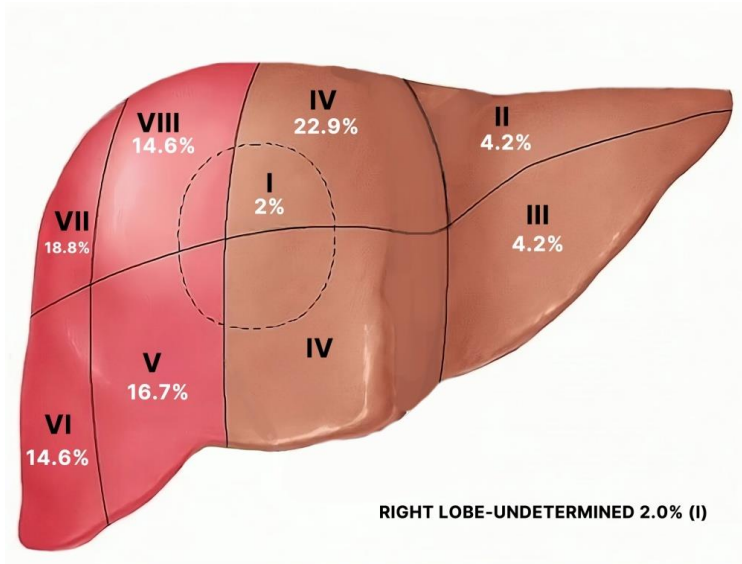


**Figure 1.** Ultrasound appearance of a typical hepatic hemangioma

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**Table 1.** Demographic characteristics

Variables		N (%)	
<b>Sex</b> (N = 567)	Male	241 (42.5)	
	Female	326 (57.5)	
<b>Age</b> (N = 567)		Mean $\pm$ SD	
	Without hemangioma	62.02 $\pm$ 13.4 years	
	With hemangioma	57.0 $\pm$ 13.4 years	
<b>Hemangioma localization</b> (N = 48)		N (%)	
	Left lobe	16 (33.3)	
	Right lobe	32 (66.7)	
<b>Patients with hemangioma</b> (N = 27)		N (%)	
	Multiple hemangiomas	13 (48.1)	
	Single hemangioma	14 (51.9)	
<b>Spleen size</b> (N = 567)		Mean $\pm$ SD	p = 0.338
	Without hemangioma	97.8 $\pm$ 14.9 mm	
	With hemangioma	95.7 $\pm$ 13.0 mm	
<b>Liver size</b> (N = 567)		Mean $\pm$ SD	p = 0.044
	Without hemangioma	131.53 $\pm$ 15.7 mm	
	With hemangioma	125.37 $\pm$ 11.3 mm	



**Figure 2.** Distribution of hepatic hemangiomas based on the liver segments

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**Table 2.** Distribution of hemangiomas according to the greatest diameter

Size of hemangioma (mm)	Frequency n (%)
< 10	16 (34.8)
10–19	21 (45.6)
20–29	7 (15.2)
30–39	1 (2.2)
> 40	1 (2.2)

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