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Seroprevalence of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus in patients undergoing nasopharyngeal biopsy** Muhammet Yildiz¹,  Erdem Atalay Cetinkaya¹,  Hulya Eyigor¹,  Omer Tarik Selcuk¹,
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We aimed to determine the seroprevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in patients undergoing nasopharyngeal biopsy (NPB). Materials and Methods: The medical records of patients who had undergone NPB under local anesthesia between 2009 and 2020 were retrospectively analyzed in our clinic. The hepatitis B surface antigen (HBsAg), HCV antibody (anti-HCV), and HIV antibody (anti-HIV) were recorded in all patients. Age, gender, and pathology result of the patients were also recorded. The patients were divided into two groups (benign and malignant) according to the pathology results. The study included 666 patients with a mean age of 38.5 ± 17.2 years (range, 6-89 years). Serology positivity was detected in 18 patients (2.7%) for HBsAg, in 4 patients (0.6%) for anti-HCV, and in 2 patients (0.3%) for anti-HIV. All serology-positive patients were older than eighteen. The HBV seropositivity rate was significantly higher in males ($p=0.003$). No statistically significant difference was found between male and female genders for HCV and HIV seropositivity ($p>0.05$). Reactive lymphoid hyperplasia (70.7%) and chronic inflammation (27.8%) were the most common results in the benign group. Undifferentiated Nasopharyngeal Carcinoma (58.9%) and B-cell non-Hodgkin lymphoma (17.8%) were the most common subtypes in the malignant group. There was no statistically significant difference between benign and malignant groups for HBV, HCV, and HIV seropositivity rates ($p>0.05$). Preoperative serological testing in patients undergoing NPB is required for increasing awareness of HBV, HCV, and HIV infections among healthcare personnels. Otolaryngologists must have the highest awareness of occupational infections deriving from blood and body fluids. It is necessary to take precaution measures including personal protective equipment during procedures..

Keywords: Hepatitis B virus, hepatitis C virus, human immunodeficiency virus, seroprevalence, nasopharyngeal biopsy**Introduction**

Blood-borne viruses (BBVs) compose various infectious agents that can be transmitted through blood and other body fluids. Twenty-six viruses are known to have caused recorded occupational infection following exposure to blood and body fluids (BBFs) among healthcare personnel (HCPs) but hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are the most common and carry a significant risk of complications [1]. Occupational exposures to BBF are the most common safety problems among HCPs [2]. It is reported that 2.5% of HIV cases and 40% of HBV and HCV cases detected in HCPs worldwide occur after occupational exposure [3].

HCPs are at risk of BBVs from occupational exposure to BBFs. Although preventing exposure is the main strategy in protecting HCPs from BBVs, exposures continue [4]. While facial exposure with BBFs was reported at high rates (34.4%), the use of facial protective equipment was detected low rates (3.7%) among HCPs [5]. Although there is a significant amount of blood splash exposure during surgical procedures, the surgeon is frequently not aware of possible infectious blood splash as notice is focused on the operation. The awareness rate of exposure to blood splash during surgery was reported to be 8.0% among surgeons [6].

ENT (Ear, Nose, Throat) surgeons by the nature of their study environment are at high risk of exposure with BBFs related infections. ENT procedures involve exposure to blood, nasal secretion, saliva, and bone dust. Additionally, a high patient cycle increases the cumulative risk even more [7]. In the current study, we aimed to investigate the seroprevalence of HBV, HCV, and HIV in patients undergoing nasopharyngeal biopsy (NPB).

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Material and Methods

The medical records of 666 patients who had undergone NPB under local anesthesia (between January 2009 and April 2020) were retrospectively analyzed in the Otorhinolaryngology Department of the Antalya Training and Research Hospital. This study was conducted following approval by the local ethics committee of Antalya Training and Research Hospital. Only patients with both a preoperative serological data and postoperative definitive histopathologic examination were included. Patients who underwent additional surgical procedures other than NPB were excluded from the study. The seropositivity of hepatitis B surface antigen (HBsAg), anti-HCV, and anti-HIV was investigated in all patients. Preoperative serological tests were studied in the microbiology clinic. Preoperative serological tests are routinely requested from patients undergoing NPB in our clinic. Age, gender, pathology result, and serological data of the patients were recorded. The patients were divided into two categories according to the pathology results (benign and malignant). We investigated the seroprevalence of antibodies against HBV, HCV, and HIV viruses among patients and to determine whether there are differences according to gender, age group, and pathology results.

Statistical Analysis

All statistical analyses were performed with SPSS version 23.0 software (IBM, Armonk, NY, USA). Descriptive analyses were presented using mean±standard deviation (SD), median (min-max), or n(%), where appropriate. The normality assumptions were controlled by the Shapiro–Wilk test. Categorical data were analyzed by Pearson chi-square and Fisher's Exact test. The differences between the two groups were evaluated with the Mann-Whitney U test for non-normally distributed data while Student's t-test was used for normally distributed data. P values < 0.05 were considered statistically significant.

Results

The study included 666 patients with a mean age of 38.5±17.2 (6-89) years. Serology positivity was detected in 18 patients (2.7%) including seventeen males and one female for HBsAg, in 4 patients (0.6%) including two males and two females for anti-HCV, and 2 patients (0.3%) including only two males for anti-HIV (Table 1). The patients were divided into two categories according to the age group: ≤18 years of age (n=89, 13.4%) (52 males, 37 females) and >18 years of age (n=577, 86.6%) (351 male, 226 female). All serology-positive patients were >18 years of age and positive for only one of these viruses.

There were 263 female and 403 male patients in our study. The HBV seropositivity rates for female patients were 0.4% (1/263) whereas the HBV seropositivity rates for male patients were 4.2% (17/403). The HBV seropositivity rate was significantly higher in males (p = 0.003). The HCV seropositivity rates for female and male patients were 0.8% (2/263) and 0.5% (2/403), respectively. HIV seropositivity was detected in only 2 male patients and its seropositivity rate was 0.5% (2/403). No statistically significant difference was found between male and female genders for HCV and HIV seropositivity (Table 2).

The patients were divided into two groups by their biopsy results: 576 (86.5%) were in the benign group and 90 (13.5%) were in the malignant group. Reactive lymphoid hyperplasia (70.7%) and chronic inflammation (27.8%) were the most common results in the benign group. Undifferentiated Nasopharyngeal Carcinoma (58.9%) and B-cell non-Hodgkin lymphoma (17.8%) were the most common subtypes in the malignant group (Table 3). In the benign group, seropositivity rates for HBV, HCV and HIV were 2.4%, 0.7% and 0.3%, respectively. Although 4.4% seropositivity was found for HbsAg in the malignant group, no seropositivity was found for HCV and HIV. There was no statistically significant difference between benign and malignant groups for these three viruses seropositivity rates (Table 4).

Table 1. Patient demographics and ELISA positivity rates (n=666)

	n	%
Age, mean±SD/ median(min-max)	38.5±17.2	37(6-89)
≤18	89	13.4
>18	577	86.6
Gender		
Female	263	39.5
Male	403	60.5
ELISA		
-	642	96.4
+	24	3.6
HBsAg	18	2.7
Anti-HCV	4	0.6
Anti-HIV	2	0.3

ELISA: Enzyme-linked immunosorbent assay; SD: Standard deviation; Min: Minimum; Max: Maximum; HBsAg: Hepatitis B surface antigen; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus.

Table 2. Comparison of ELISA positivity rates between genders

	Female	Male	p
Age, mean±SD/ median(min-max)	38±17.1/36 (13-89)	38.7±17.4/37 (6-86)	0.615*
n(%)			
-	260(98.9)	382(94.8)	0.006 ⁺
+	3(1.1)	21(5.2)	
HBsAg	1(0.4)	17(4.2)	0.003 ⁺
Anti-HCV	2(0.8)	2(0.5)	0.649°
Anti-HIV	0(0)	2(0.5)	0.521°

Data are presented as mean±SD, median (min-max) and n (%). ELISA: Enzyme-linked immunosorbent assay; SD: Standard deviation; Min: Minimum; Max: Maximum; HBsAg: Hepatitis B surface antigen; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus. *Student's t test, ⁺Pearson chi-square test, ° Fisher's Exact test.

Table 3. Distribution of patient corresponding of biopsy results.

Results of Biopsy	n	%
Benign	576	86.5
Reactive lymphoid hyperplasia	407	70.7
Chronic inflammation	160	27.8
Thornwaldt's cyst	5	0.9
Granulomatous lesion	3	0.5
Nasopharyngeal Angiofibroma	1	0.2
Malignant	90	13.5
Non-Keratinizing Undifferentiated Nasopharyngeal Cancer	53	58.9
Non- Keratinizing Differentiated Nasopharyngeal Cancer	4	4.4
Keratinizing Nasopharyngeal Cancer	7	7.8
B-Cell Non-Hodgkin Lymphoma	16	17.8
T-Cell Non-Hodgkin Lymphoma	3	3.3
Hodgkin Lymphoma	3	3.3
Malignant Small Round-Cell Tumor	2	2.2
Nasopharyngeal Chordoma	1	1.1
Metastatic Gastric Signet-Ring Cell Carcinoma	1	1.1

Table 4. Comparison of ELISA positivity rates in benign and malignant groups

	Benign	Malignant	p
n(%)			
-	556(96.5)	86(95.6)	0.552
+	20(3.5)	4(4.4)	
HBsAg	14(2.4)	4(4.4)	0.287
Anti-HCV	4(0.7)	0(0)	0.999
Anti-HIV	2(0.3)	0(0)	0.999

Data are presented as n (%). ELISA: Enzyme-linked immunosorbent assay; HBsAg: Hepatitis B surface antigen; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus. Fisher's Exact test.

Discussion

HCPs are exposed to biological dangers deriving from BBFs on daily practice, because of occupational accidents that can occur from percutaneous injuries, mucocutaneous injuries (splattering of BBFs into the eyes, nose, or mouth) or blood contact with damaged skin [8,9]. HBV, HCV, and HIV are extensive causes of occupational illness transmitted from patients to HCPs. These infections can lead to considerable problems, including long-term illnesses, disability, and death [10].

HCPs have an increased risk of infection due to direct contact with patients or their infective materials [11]. HCPs are exposed to dangerous BBVs including HBV, HCV, and HIV in their working

environment. The presence of these viruses was shown in saliva and nasal secretion of HBV, HCV, and HIV positive patients [12-14]. HIV RNA was also detected in nasopharyngeal washes from patients with detectable plasma viral load [15]. These findings have implications for the potential transmission of HBV, HCV, and HIV through contact with contaminated saliva and nasal secretion. Surgical procedures significantly increase exposure to pathogenic viruses that facial exposure to BBFs is shown an important risk factor for the transmission of BBVs [16,17]. HCV and HIV transmission have been shown with the presence of a sufficient amount of infective particles on the mucous membranes [18,19].

All surgeons are particularly at risk from blood-borne pathogens during interventions or surgeries, but ENT surgeons are particularly at high risk of exposure with BBF related infections both in outpatient and during surgical procedures. Although surgeons take precautions against sharp instrument injuries, they do not show the necessary care against protection from BBF splashes into eyes, nose, or mouth [7,20]. The study performed by Shrestha et al. [21] showed that an overall 41.9% risk of blood splashes on the protective glass during surgery for the surgeon. Whereas 38.9% risk in mask and 23.5% risk in a gown for the surgeon. This study states that there is a significant number of blood splashes to the ENT surgeon during ENT operations [21]. The prevalence of HIV and hepatitis is increasing, so there is always the risk of transmission of disease in HCPs. Therefore, it is necessary to take protective measures by the HCPs during the operation of patients or any other interventional procedure to avoid unnecessary contamination with the patient's BBFs.

Lakhani et al. [7] investigated the degree and incidence of blood splashes in otolaryngology procedures. Tonsillectomy (76.9 %) and rhinology procedures (47 %) have significant splash rates. In 54 % of the operations, a certain amount of blood spatter was also detected. In terms of blood spatter rates, they did not find a statistically significant difference between the operations with and without local infiltration. Additionally, they did not find a relationship between the rate of blood spatter and blood loss or duration of the operation or experience of the surgeon [7].

Developing countries have higher rates for the transmission of BBVs, particularly for occupational exposure [22]. The seroprevalence positivity rates were found to be 3.6% for HBV, 0.3% for HCV, and 0.2% for HIV in patients undergoing septoplasty [23]. Additionally, the seroprevalence positivity rates were found to be 1.5% for HBV, 0.2% for HCV, and 0.2% for HIV in patients undergoing tonsillectomy [24]. The seropositivity rates of Turkey (a developing country) were previously reported as 0.52 to 4.19% for HBV, 0.1 to 1% for HCV, and 0 to 0.1% for HIV [25,26]. Among our patient population, positive serology for HBV was detected in 18 (2.7%) and four patients (0.6%) had HCV positivity, while two other patients (0.3%) had HIV positivity. Our seroprevalence results are also consistent with these findings. According to the age groups, >18 years of age was associated with a higher possibility of such an occupational spread. Besides, the HBV positivity was higher in males.

The associations of HBV infection with nasopharyngeal cancers (NPCs) are interesting. Interaction with the Epstein Barr virus is emphasized in explaining the relationship between HBV and NPC

[27]. HBV positivity was demonstrated in approximately 11 % of patients with NPCs [28]. In another study, HBV seropositivity was reported as 1.8% in 1165 NPC cases aged ≥ 66 years [29]. Reactivation may occur after chemotherapy in patients infected with HBV [30]. Another study has shown that HBV positivity may have an impact on NPC prognosis [31]. In our study, 4.4% seropositivity was found for HBV in the nasopharyngeal malignancy.

In our clinic, NPB is often performed with local anesthesia. In this procedure, local anesthesia is a very reliable and inexpensive method in cases where the pain is reduced or prevented during the operation [32]. HBV, HCV, and HIV serological tests are always requested from all patients undergoing NPB in our clinic. However, in some clinics in our country, this procedure can be performed without requiring preoperative serological examinations for various reasons. NPB is often performed under local anesthesia, and if the patient does not have adequate pain control, involuntary sudden movements of the patient may cause contact with the patient's BBFs. Besides, the patient's cough or sneezing after the pain and bleeding during the procedure may increase the likelihood of transmission of blood-borne infection [21,23]. Due to all these risk factors, ENT surgeons increase the likelihood of contact with the patient's BBFs, and therefore the risk of transmission of blood-borne infection from seropositive patients also increases. During the NPB procedure, the ENT surgeon may be exposed to BBFs, resulting in significant risk of transmission, therefore we emphasize that serological tests should be routinely requested from patients undergoing NPB with local anesthesia.

In the management of occupational infectious diseases and to develop appropriate behaviors, it is significant for HCPs to know the risk of infection, transmission routes, and possibly avoiding methods [33]. Because of the silent course of these diseases, chronic infections can progress unnoticed for years. As a result, the vast majority of chronically infected patients may not be aware of their illness and therefore do not receive appropriate care [34]. Requesting preoperative serological tests from patients can ensure that all HCP, especially the surgeon, take additional caution during the procedure. It also provides an early diagnosis in non-diagnosed patients and reducing disease spread. In our study, one of two HIV seropositive patients, one of four HCV seropositive patients, and seven of eighteen HBV seropositive patients were not diagnosed until the time of preoperative testing which we did before NPB.

HCPs must have the highest awareness of biological dangers deriving from BBFs. Personal protective equipment (masks, gloves gowns, goggles, or face shields) should be used to prevent BBVs and safe working techniques should be developed [35,36]. Vaccination against HBV and preoperative tests for seropositivity can also prevent spread [37].

Conclusion

Preoperative HBV, HCV, and HIV serological tests should be routinely requested from patients over 18 years of age to undergo NPB. In this study, we state that the ENT surgeons may have an increased risk for infections transmitted by BBFs during the NPB procedure, which is frequently performed in polyclinics and operating rooms. Additionally, all ENT surgeons should be

careful about blood-borne infections and use personal protective equipment during the NPB procedure.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

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Ethical approval

Approval for the study was granted by the Local Ethics Committee of Antalya Training and Research Hospital.

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