Analysis of the epidemiological profile of Hepatitis B cases in the metropolitan region of São Paulo from 2010 to 2020

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ABSTRACT

This study evaluates the epidemiological profile of patients with Hepatitis B in the Metropolitan Region of São Paulo (MRSP), notified between 2010 and 2020. Secondary data were collected through the Notifiable Diseases Information System of the Ministry of Health (SINAN) and analyzed through a descriptive cross-sectional study. The determinants used to study the prevalence of the disease were gender, age group, race, and area of residence. A total of 1,384 cases were reported, with a predominance of cases in males (71.96%; n=996), aged 20 to 39 years (52.67%; n=729), self-declared white race (45.66%; n=632), with the city of São Paulo being the region with the highest prevalence of the disease (74.20%; n=1,027). The evaluation of the variables schooling and mechanism of infection were impaired due to incomplete completion or non-completion of the field in the notification forms. The present study aims to identify high-risk groups, outlining etiological hypotheses for prevention purposes and future investigations.

Keywords: Hepatitis B, Epidemiological profile, Public health.

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INTRODUCTION

The Metropolitan Region of São Paulo (MRSP) is made up of 39 municipalities that form the largest urban agglomeration in South America, and the sixth largest in the world, totaling a population of 20 million inhabitants (São Paulo, 2022). These data suggest the diversity present in the region in terms of access to health services, and the different sociodemographic and cultural characteristics of the population. Viral hepatitis represents one of the main impasses for public health, and its occurrence and aggravations are related to a series of factors that involve educational, social, cultural, and economic issues. However, many individuals living with hepatitis do not have access to hepatitis prevention and treatment services. The present study aims to identify high-risk groups, outlining etiological hypotheses for prevention purposes and future investigations.

As will be seen, the Hepatitis B virus (HBV) is transmitted through skin and mucosal lesions, unprotected sexual intercourse, percutaneous exposure to contaminated needles or other sharp instruments, injection drug use, perinatal transmission, and through household contacts in overcrowded environments. It is also transmitted by procedures that disregard universal biosafety standards. In addition to the general prevalence in the population, individuals who constitute risk groups and those with different pathological conditions should be evaluated.

The prevalence of hepatitis in people in situations of social vulnerability and low economic status will also be analyzed, who, in general, have restricted access to public health services, and their diagnosis is made only in more advanced stages of the disease.

Through the monitoring of infected individuals, relevant information will be demonstrated to reliably identify HBV infections, as well as the stage of the disease and its clinical manifestations. The lack of information causes a concomitant effect with lower adherence to the vaccine against the virus and, therefore, the incidence rate remains high even in large urban centers. The present study will evaluate data from 39 municipalities that feed the MRSP, verified by the section "Notifiable Diseases and Diseases - 2007 onwards (SINAN)" for the disease Hepatitis B, which is a notifiable disease throughout the national territory. Viral hepatitis comprises a group of diseases with a great capacity for infiltration and proliferation by liver tissue, which have a high number of occurrences and clinical manifestations.

DEVELOPMENT

THE VIRUS

After the presentation of the Hepatitis B vaccine in Brazil, the epidemiological profile of this virus has been changing. Lopes and Schinoni (2011) argue that HBV, belonging to the *Hepadnaviridae* family, is an enveloped virus with an affinity for liver cells. HBV is transmitted through skin and mucosal lesions, sexual intercourse, and exposure to contaminated materials. Blood

transfusion, dental, surgical and hemodialysis procedures, which do not comply with universal biosafety standards, are still reported routes of transmission. In addition, injecting drug use, perinatal transmission, and household contacts in overcrowded environments are also reporting variables. According to Chávez, Campana and Haas (2003), in the general population, this virus preferentially affects individuals in the age group of 20 to 59 years.

The clinical manifestations of hepatitis are extremely varied, ranging from an asymptomatic infection to a potentially serious disease with fulminant evolution (DE SOUSA, 2014). About 1 to 2% of acute cases may present severe forms such as fulminant hepatitis or sub-fulminant necrosis (LOPES; SCHINONI, 2011). Symptoms during the pre-jaundiced period may include fever, arthralgias, anorexia, malaise, nausea, emesis, myalgias, and fatigue, as well as signs such as lymphadenopathy, leukopenia, proteinuria, and skin rash; changes in taste and smell, pain in the right hypochondrium or epigastralgia can also be found (DE SOUSA, 2014). The author also mentions that jaundice predominates in the jaundice phase, and the same symptoms as in the previous phase with intensification, with dysgeusia and involuntary weight loss may occur.

Epidemiology

Epidemiological studies on hepatitis B in Brazil are deficient and prevalent in specific groups (FERREIRA; SILVEIRA, 2004). When analyzing the distribution of cases by Brazilian region, it was possible to observe that cases are more evident in the Southeast (40%) and less frequent in the Midwest (7%), and the South and Southeast regions had the highest number of diagnosed cases, probably due to a better epidemiological surveillance system (TIMÓTEO, *et al*, 2020), and more than 80% of people living with hepatitis lack prevention services, testing and treatment.

Natural History of the Disease

De Sousa (2014) describes that hepatitis B has distinct phases, initiated by the immunotolerance phase, which is characterized by great viral replication, while the immune system tolerates this replicative capacity. The author also explains that in the Immuno-Clearance phase, there is a decline in immunity, resulting in aggression to hepatocytes and elevation of transaminases. According to the Ministry of Health in Ordinance No. 2,561 of 2009, the state of inactive carrier is characterized by very low or undetectable levels of viral replication and normalization of liver enzymes, which indicates immune control over the virus, although immune escape may occur. Its reactivation occurs during immunosuppression, either by chemotherapy, immunosuppressants or viral mutations, allowing viral replication by escaping the host's immune surveillance.

Prevention and Vaccine

Initially, it should be noted that individuals who constitute risk groups and also those who present different pathological conditions, such as perinatal infection, acute and chronic hepatitis, asymptomatic carriers of the B virus, cirrhotic patients and patients with hepatocellular carcinoma, are usually underreported by SINAN. Ferreira and Silveira (2004) contemplate strategies used to eliminate viral transmission, which consist of four components: (1) prevention of perinatal infection, through maternal screening and post-exposure prophylaxis of HBsAg-positive mothers; (2) vaccination against hepatitis B of all children, with a view to preventing infection in childhood and at an older age; (3) vaccination of adolescents who were not protected; (4) vaccination of individuals belonging to risk groups.

Occasionally, contamination is described in hospitals, and it can be transmitted between patients, through contaminated equipment, multipurpose drug bottles, organ transplants, among others (FERREIRA; SILVEIRA, 2004). With regard to the surveillance of chronic liver diseases, Ferreira and Silveira (2004) describe that "the positive HBsAg marker is of great value", and can be detected in all cases of chronic hepatitis, facilitating referral to diagnostic and treatment centers and also enabling the immunization of contacts.

METHODOLOGY

STUDY DESIGN

This is a descriptive cross-sectional study on the clinical-epidemiological profile of Hepatitis B cases in the Metropolitan Region of São Paulo (MRSP), reported between 2010 and 2020. The data, of secondary origin, were obtained from the Notifiable Diseases Information System of the Ministry of Health (SINAN), a system that is part of the database of the Department of Informatics of the Unified Health System (MINISTRY OF HEALTH).

SOURCE AND COLLECTION OF SURVEY DATA

The data of the 39 municipalities that feed the MRSP were verified in the section "Notifiable Diseases and Diseases - 2007 onwards (SINAN)" of the "Epidemiological and Morbidity" tab, followed by the option "Hepatitis" in the geographic coverage of "São Paulo".

ANALYSIS PLAN

Data filtered by their etiological classification only for the Hepatitis B virus and reactive serology were included, through laboratory and clinical-epidemiological confirmation and serological scarring. The selected regions were determined by "Municipality of Residence", and their

determinants used to study the prevalence of Hepatitis B were sex, age group, race and area of residence.

Data analysis and organization were performed using Microsoft Office Excel 365 and TabNet Win32 3.2 programs, available free of charge through the website of the Department of Informatics of the Unified Health System (MINISTRY OF HEALTH).

ETHICAL ASPECTS

This project is in accordance with the terms of Resolution 466/12 of the National Health Council (2012), since the secondary data used in its development were obtained through the consultation source and public domain Department of Informatics of the Unified Health System (MINISTRY OF HEALTH), not requiring consideration by the Research Ethics Committee.

STUDY POPULATION

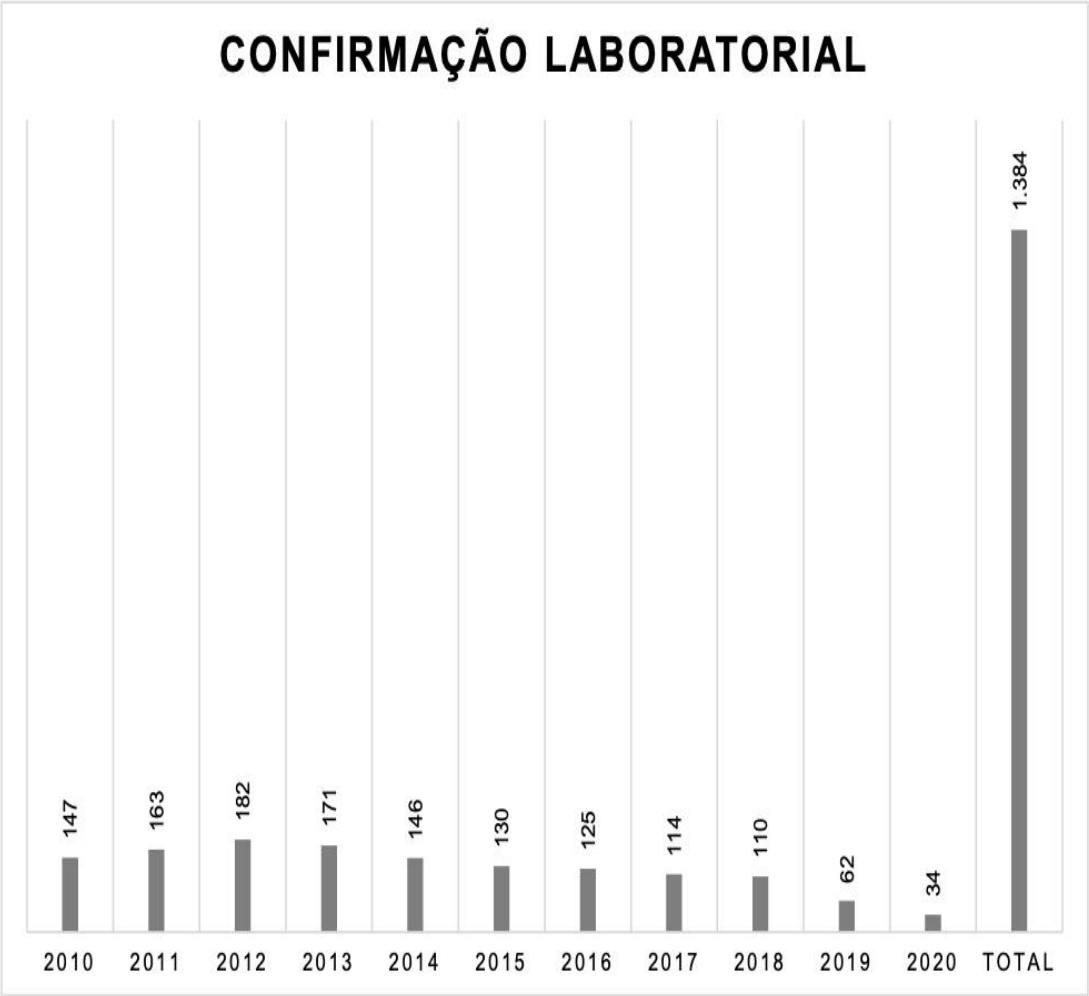
The incidence rate of Hepatitis B cases was calculated as the number of new cases of the disease (through laboratory confirmation, clinical-epidemiological confirmation and serological scarring) divided by the population residing in the place and year, multiplied by 100 thousand inhabitants, according to Formula 1, described by Böhm (*et al*, 2016), below:

Formula 1 - Calculation of the incidence rate per 100 thousand inhabitants.
Incidence rate = (number of new cases-year/study population) x 100,000
Source: Böhm, Costa, Neves, Flores & Nunes (2016).

RESULTS

In the Metropolitan Region of São Paulo, the total number of cases with laboratory, clinical-epidemiological confirmation and serological scarring from 2010 to 2020 was 1,384, with an annual average of 125 cases per year, with a variation of 34 cases (2020) and 182 (2012), as observed in Figure 1:

Figure 1 - Number of laboratory confirmation of Hepatitis B cases reported from 2010 to 2020 in the municipalities belonging to the Metropolitan Region of São Paulo.



Source: Authored by the author based on data collected through the Ministry of Health/SVS - Notifiable Diseases Information System.

The prevalence of cases corresponds to an incidence rate of 2,456 cases per 100,000 inhabitants in 2020 and 13,150 cases per 100,000 inhabitants in 2012, as shown in table 1:

Table 1 – Notifications of hepatitis B in the period from 2010 to 2020 in the municipalities belonging to the Metropolitan Region of São Paulo.

Município de notificação	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	TOTAL	População*	Taxa**	%***
TOTAL	147	163	182	171	146	130	125	114	110	62	34	1.384	19.683.975		
BARUERI	1	2	1	1	1	2	2	-	2	1	-	13	240.749	5,39	0,93
CAIEIRAS	-	1	2	2	-	1	-	-	1	-	-	7	86.529	8,08	0,50
CAJAMAR	1	-	-	-	-	-	-	1	-	-	-	2	64.114	3,11	0,14
CARAPICUÍBA	2	1	3	-	3	-	12	1	2	1	2	27	369.584	7,30	1,90
COTIA	2	-	1	1	3	3	1	-	1	-	-	12	201.150	5,96	0,86
DIADEMA	1	5	9	7	7	4	7	1	7	2	1	51	386.089	13,2	3,68
EMBU DAS ARTES	-	1	5	-	-	-	-	-	-	-	-	6	240.230	2,49	0,43
EMBU-GUAÇU	-	-	-	-	-	-	-	-	-	-	1	1	62.769	1,59	0,07
FERRAZ DE VASCONCELOS	-	-	-	1	-	-	1	-	-	1	-	3	168.306	1,78	0,21
FRANCISCO MORATO	-	1	1	1	4	1	-	-	1	-	-	9	154.472	5,82	0,65
FRANCO DA ROCHA	-	-	1	1	-	1	-	1	-	-	1	5	131.604	3,79	0,36
GUARAREMA	-	1	-	-	-	-	-	-	-	-	-	1	25.844	3,86	0,07
GUARULHOS	6	6	5	11	3	4	11	1	6	1	2	56	1.221.979	4,58	4,04
ITAPECERICA DA SERRA	-	1	-	-	-	1	-	-	-	-	-	2	152.614	1,31	0,14
ITAPEVI	2	-	2	1	2	2	-	-	1	1	-	11	200.769	5,47	0,79
ITAQUAQUECETUBA	1	1	-	2	-	-	-	-	1	1	-	6	321.770	1,86	0,43
JANDIRA	1	-	3	1	1	-	-	-	-	-	-	6	108.344	5,53	0,43
MAUÁ	1	3	-	2	-	3	1	2	1	-	-	13	417.064	3,11	0,93
MOGI DAS CRUZES	-	1	2	-	2	5	5	3	1	4	1	24	387.779	6,18	1,73
OSASCO	3	4	7	2	2	2	2	-	-	-	-	22	666.740	3,29	1,58
RIBEIRÃO PIRES	-	-	1	1	-	-	-	-	-	-	1	3	113.068	2,65	0,21
SANTANA DE PARNAÍBA	-	1	2	-	2	-	-	1	-	-	-	6	108.813	5,51	0,43
SANTO ANDRÉ	2	1	3	3	2	1	1	1	2	1	-	17	676.407	2,51	1,22
SÃO BERNARDO DO CAMPO	5	1	3	-	2	-	2	3	3	3	1	23	765.463	3,00	1,66
SÃO CAETANO DO SUL	-	1	2	1	1	-	1	-	-	-	1	7	149.263	4,68	0,50
SÃO LOURENCO DA SERRA	-	-	-	-	-	1	-	-	-	-	-	1	13.973	7,15	0,07
SÃO PAULO	118	129	125	129	106	97	78	98	80	46	21	1.027	11.253.503	9,12	74,2
SUZANO	1	1	1	2	1	1	1	1	-	-	2	11	262.480	4,19	0,79
TABOÃO DA SERRA	-	1	3	2	4	1	-	-	1	-	-	12	244.528	4,90	0,86

*Resident population by municipality in 2010, according to the Brazilian Institute of Geography and Statistics (IBGE).
**n: Incidence rate of Hepatitis B cases per 100,000 inhabitants.
%: Percentage relative to the number of cases reported per municipality in relation to the total number of cases.
Source: Authored by the author based on data obtained from the Ministry of Health/SVS - Notifiable Diseases Information System.

Regarding the distribution of cases by municipality, 10 of the 39 municipalities (Arujá, Biritiba-Mirim, Juquitiba, Mairiporã, Pirapora do Bom Jesus, Poa, Rio Grande da Serra, Salesópolis, Santa Isabel, Vargem Grande Paulista) did not report cases of Hepatitis B in the period from 2010 to 2020. The city of São Paulo had the highest number of notifications, with 1,027 cases (74.20% of the total cases), which is equivalent to 9.12 cases per 100 thousand inhabitants. During the same period, Diadema with 51 cases (3.68%), Guarulhos with 56 cases (4.04%), and the rest of the municipalities with 247 cases (17.84%) accumulated. The municipalities of Embu-Guaçu, Guararema and São Lourenço da Serra each had 1 case during the study period (0.07%), and a total incidence rate of 12.6 cases per 100 thousand inhabitants.

During the period from 2010 to 2020, 946 cases of Hepatitis B were reported in the municipality of São Paulo alone (68.35%), 68 cases in Guarulhos (4.91%), 52 cases in Diadema (3.75%), 37 cases in Carapicuíba (2.67%), 34 cases in Osasco (2.45%), and 247 in the rest of the municipalities (17.84%), as shown in Table 1.

Males accounted for 996 cases (71.96%), while females reported 388 cases (28.03%), with a predominance of male cases in the city of São Paulo, with 706 cases (51.01% of the total), and 240 females (17.34% of the total).

Regarding the age group, the highest number reported was 729 in the age group of 20 to 39 years (52.67% of the total), 491 in the age group of 40 to 59 years (35.47% of the total), 61 cases in the age group of 60 to 64 years (4.40% of the total), 38 cases in the age group of 65 to 69 years (2.74% of the total), 27 cases between 15 and 19 years old (1.95% of the total), 26 cases between 70 and 79 years old (1.87% of the total), and the rest accounting for 12 cases (0.86% of the total).

The variable "Skin color or race" had its highest number of notifications in the self-declared group of "White" with 632 cases (45.66%), followed by 413 in "Brown" (29.84%), 161 records with incomplete field registered as "Unknown/White" (11.63%), 137 in "Black" (9.89%), 36 in "Yellow" (2.60%) and 5 in "Indigenous" (0.36%).

Regarding the level of education, 398 cases were registered with the "Unknown/White" field (28.75%), followed by 308 with "Complete High School" (22.25%), 134 with "5th to 8th incomplete grade of PE" (9.68%), 123 with "Complete Higher Education" (8.88%), 120 with "Complete Elementary School" (8.67%), 100 with "Incomplete High School" (7.22%), and 201 cases in the other (14.52%) items "Illiterate", "1st to 4th grade incomplete", "4th grade complete", "Higher Education incomplete" and "Not applicable", as shown in Table 2:

Table 2 – Profile of hepatitis B notifications from 2010 to 2020 in the municipalities belonging to the Metropolitan Region of São Paulo.

Variable	**n***	**%****
Gender		
Male	996	71,96
Female	388	28,03
Age group		
< 1 year	2	0,14
1 a 4	2	0,14
5 a 9	1	0,07
10 a 14	1	0,07
15 a 19	27	1,95
20 a 39	729	52,67
40 a 59	491	35,47
60 a 64	61	4,40
65 a 69	38	2,74
70 a 79	26	1,87
> 80	6	0,43

Skin Color/Race		
Yellow	36	2,60
White	632	45,66
Indigenous	5	0,36
Curtain	413	29,84
Black	137	9,89
Ignored/Blank	161	11,63
Schooling		
Illiterate	10	0,72
1st to 4th grade incomplete EF	66	4,76
Complete EF 4th Series	45	3,25
5th to 8th grade incomplete EF	134	9,68
Complete elementary school	120	8,67
Incomplete high school	100	7,22
Completed high school	308	22,25
Incomplete higher education	74	5,34
Completed higher education	123	8,88
Not applicable	6	0,43
Ignored/White	398	28,75
TOTAL	1.384	100,00

* n: Total number of cases reported in the period from 2010 to 2020.
**%: percentage relative to the number of reported cases per group in relation to the total number of cases.
Source: Authored by the author based on data obtained from the Ministry of Health/SVS - Notifiable Diseases Information System.

Among the mechanisms of infection, 782 records were registered with the "Unknown/Blank" field (56.50%), 435 by "Sexual" route (31.43%), 54 by "Injection Drug Use" (3.90%), 45 by "Dental Treatment" (3.25%), 26 notified as "Other" (1.87%), 12 cases by "Transfusion" route (0.86%), 10 cases by "Home" (0.72%), and the remainder were 20 cases (1.44%) by "Vertical" route. "Occupational Accident", "Hemodialysis", "Surgical Treatment" and "Person/person", as shown in Table 3:

Table 3 - Source/Mechanism of Infection of Hepatitis B cases reported from 2010 to 2020 in the Municipalities belonging to the Metropolitan Region of São Paulo.

Mec. Infection	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	n*	%**
Ignored/White	72	89	98	103	81	66	77	74	63	40	19	782	56,50
Sexual	57	52	55	54	46	44	31	34	34	17	11	435	31,43
Transfusional	2	-	4	3	1	1	1	-	-	-	-	12	0,86
Injectable Drugs	8	6	11	3	-	5	8	4	3	3	3	54	3,90
Vertical	-	-	-	-	1	-	-	-	-	-	-	1	0,07
Accident at Work	-	1	-	-	-	2	1	-	-	-	-	4	0,28
Hemodialysis	-	-	-	-	-	-	1	-	-	-	-	1	0,07
Home	1	1	2	2	-	2	2	-	-	-	-	10	0,72
Surgical Treatment	-	1	2	2	-	-	-	-	1	1	-	7	0,50
Dental Treatment	7	9	5	4	7	3	4	1	5	-	-	45	3,25
Person/Person	-	1	2	-	2	1	-	-	1	-	-	7	0,50
Other	-	3	3	-	8	6	-	1	3	1	1	26	1,87
TOTAL	147	163	182	171	146	130	125	114	110	62	34	1.384	100,00

*n: Total number of cases reported from 2010 to 2020.
** %: Percentage relative to the number of reported cases per group in relation to the total number of cases.
Source: Authored by the author based on data obtained from the Ministry of Health/SVS - Notifiable Diseases Information System.

DISCUSSION

Based on the data extracted in the present study, the epidemiological profile of Hepatitis B cases in the Metropolitan Region of São Paulo from 2010 to 2020 was analyzed, through the determinants: sex, age group, race, education, and infection mechanism. The prevalence of notifications was noted in the municipality of São Paulo (74.20%), in males (71.96%) and Caucasians (45.66%), and that the incidence rate decreased significantly in 2020. In addition, it was evidenced that the highest number of notifications of the means of transmission of the disease were identified as "Ignored/Blank" by SINAN, as predicted in the literature (Timóteo et al. 2020).

The age group most affected by the Hepatitis B virus was 20 to 39 years, with 52.67% of notifications, and 40 to 59 years, with 35.47% (Table 2), which includes the sexually active population (31.43%) observed in Table 3. It was also observed that in 2020 the number of confirmed cases of injecting drug use is significantly lower compared to 2011, but still suggests the inefficiency of harm reduction programs, since this is a group of extreme social vulnerability. On the other hand,

cases of transmission via Transfusion, Work Accident, Vertical, Home and Hemodialysis were not quantified from 2017 to 2020.

Regarding the variable "Skin color/Race", the self-declared color groups "White" (45.66%) and "Brown" (29.84%) had the highest values, followed by those with incomplete completion in "Unknown/White" (11.63%), "Black" (9.89%), "Yellow" (2.60%) and "Indigenous" (0.36%).

The variable "Schooling" was selected for a possible relationship between epidemiological profile and level of education, but the largest number reported had this field ignored or not filled in ("Ignored/Blank"), thus losing the information necessary for the study. These data, therefore, do not match the epidemiological situation of the region, so that the planning of measures for the prevention and control of the disease is impaired. For the correctly filled out forms, the largest number of individuals had completed high school, however, the confirmation of the incidence associated with low schooling was not confirmed.

In agreement with Gusmão's study (*et. al.,* 2017), the prevalence of the disease in males is related to higher risk behavior. Although sexual transmission is predominant in this study, corresponding to 31.43% (n=435) of the cases, it was not possible to determine the main mechanism of infection, since 56.50% (n=782) of the forms did not contain the filled field ("Ignored/Blank"). This data interferes in the correct determination of the main Infection Mechanism in the region, and warns about the large number of incomplete completion of notification forms by health professionals.

CONCLUSION

The Metropolitan Region of São Paulo is the largest urban agglomeration in South America, and Hepatitis B has been shown to be a problem of great relevance for public health, since the region has different sociodemographic and cultural characteristics. The lack of information about Hepatitis B and the large number of incomplete notifications are causes related to non-immunization against the disease. In addition, it represents one of the main impasses for public health, since it is not possible to correctly identify the etiological hypotheses and the groups at greatest risk.

The present study concluded that the city of São Paulo had the highest number of notifications during the period studied, as well as males in the most sexually active age group. This is possibly due to unprotected sexual activity and inefficient self-care practices compared to females.

The variables "Schooling" and "Mechanism of Infection" were impaired due to incomplete completion or non-completion of notification forms. The underreporting of data requested in the forms impedes the global characterization of the profiles of individuals with hepatitis B.

In addition, the variable "Skin Color/Race" proves that there is a structural problem related to access to health care within the population declared "Black", since the data represent the social phenomena of racial inequality that have prevailed throughout the history of Brazil.

REFERENCES

1. Böhm, A. W., Costa, C. S., Neves, R. G., Flores, T. R., & Nunes, B. P. (2016). Tendência da incidência de dengue no Brasil, 2002-2012. Epidemiologia e Serviços de Saúde, 25(4). Recuperado de https://www.scielo.br/j/ress/a/DVxtRGwmTrGb3sSFnZdLLpb/?format=pdf&lang=pt

2. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. (2009). Portaria n˚ 2.561, de 28 de outubro de 2009. Protocolo Clínico e Diretrizes Terapêuticas - Hepatite Viral Crônica B e Coinfecções. Recuperado de https://bvsms.saude.gov.br/bvs/saudelegis/gm/2009/prt2561_28_10_2009.html

3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. (s.d.). Sistema de Informação de Agravos de Notificação - Sinan Net. Recuperado de http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinannet/cnv/hepasp.def

4. Chávez, J. H., Campana, S. G., & Haas, P. (2003). Panorama da hepatite B no Brasil e no Estado de Santa Catarina. Revista Panamericana de Salud Pública, 14(2), 91-96. Recuperado de https://www.scielosp.org/pdf/rpsp/v14n2/a03v14n2.pdf

5. Conselho Nacional de Saúde. (2012). Resolução n˚ 466, de 12 de dezembro de 2012. Recuperado de https://conselho.saude.gov.br/resolucoes/2012/Reso466.pdf

6. de Sousa, T. F. (2014). Hepatites virais–uma revisão de literatura. Brazilian Journal of Surgery and Clinical Research - BJSCR, 5(1), 55-58. Recuperado de https://www.mastereditora.com.br/periodico/20140429_213345.pdf

7. Ferreira, C. T., & Silveira, T. R. da. (2004). Hepatites virais: aspectos da epidemiologia e da prevenção. Revista Brasileira de Epidemiologia, 7(4), 473-487. Recuperado de https://www.scielosp.org/pdf/rbepid/v7n4/10.pdf

8. Gusmão B. M., Pereira F. S., Rocha A. P., Fernandes M. B. da S., Dias O. V., & Costa S. D. M. (2017). Análise do perfil sociodemográfico de notificados para hepatite B e imunização contra a doença. Revista Pesquisa (Univ. Fed. Estado Rio J., Online), 9(3), 627-633. Recuperado de https://seer.unirio.br/cuidadofundamental/article/view/5550

9. Lopes, T. G. S. L., & Schinoni, M. I. (2011). Aspectos gerais da hepatite B. Recuperado de https://repositorio.ufba.br/handle/ri/5715

10. Ministério da Saúde. DATASUS. (2022). Tabnet. Recuperado de https://datasus.saude.gov.br/

11. São Paulo, Prefeitura Municipal de. (2022). População Recenseada, Região Metropolitana de São Paulo e Municípios, 1950, 1960, 1970, 1980, 1990, 2000, 2010 e 2022. Recuperado de https://www.prefeitura.sp.gov.br/cidade/secretarias/upload/chamadas/tabela_pop_municipios_rsmp_evol_1950-2022_1698773663.htm

12. Timóteo, M. V. F., Araujo, F. J. da R., Martins, K. C. P., Silva, H. R. da, Silva Neto, G. A. da, Pereira, R. A. C., Paulino, J. de S., Pessoa, G. T., Alvino, V. de S., & Costa, R. H. F. (2020). Epidemiological profile of viral hepatitis in Brazil. Research, Society and Development, 9(6), e29963231. https://doi.org/10.33448/rsd-v9i6.3231. Recuperado de https://rsdjournal.org/index.php/rsd/article/view/3231