Journal of Infection and Public Health 12 (2019) 516–521

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Validity of hepatitis B and hepatitis C case definitions

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ARTICLE INFO

Article history:
Received 24 January 2018
Received in revised form 28 May 2018
Accepted 22 January 2019

Keywords:
Hepatitis B & C
Surveillance
Case definition
Sensitivity and specificity
Serbia

ABSTRACT

Background: Globally, an estimated 257 million people are living with chronic hepatitis B (HBV) infection and an estimated 71 million people with the chronic hepatitis C virus (HCV). The true public health dimensions and impact of hepatitis epidemics are poorly understood. Case definitions are fundamental parts of disease surveillance, representing sets of standardised criteria used to assess whether or not a person has a certain disease. The study evaluated the sensitivity and specificity of hepatitis B and hepatitis C case definitions, current at the time of data collection, recommended by the European Commission (EC) and the Centers for Disease Prevention and Control (CDC).

Methods: The study involved 150 hospital referrals with suspected cases of hepatitis from a Serbian clinic during 2014/2015. Case definitions of hepatitis B and C were tested for their sensitivity, specificity, positive and negative predictive values.

Results: EC 2008 and the CDC 2012 case definitions for acute hepatitis B, and the CDC 2012 case definition for probable case of chronic hepatitis B have low sensitivity. Case definitions which rely on laboratory confirmation only have maximal sensitivity. EC case definitions showed maximal sensitivity and specificity for hepatitis C confirmed cases. The CDC case definition for chronic hepatitis C showed low sensitivity (36.8%) and low negative predictive value (65.6%) for probable cases and maximal sensitivity and specificity for confirmed cases. Hepatitis C case definitions requiring presence of clinical criteria have low sensitivity and high specificity, resulting from presence of infection and absence of any clinical manifestation, but have high positive and negative predictive values.

Conclusion: Syndromic case definitions show low sensitivity and are of limited use. They highlight the importance of laboratory diagnostics (offering maximal sensitivity and specificity, and high positive and negative predictive values), as well as the need for universal case definitions, for confirmed cases only.

Introduction

In 2016, the World Health Organisation published their global health sector strategy on viral hepatitis [1], outlining a goal of eliminating it as a major public health threat by 2030. It also provides targets seeking to reduce the incidence of chronic hepatitis infection, and the annual deaths from chronic hepatitis, which will require a radical change in the hepatitis response. It is estimated that 257 million people are living with chronic hepatitis B (HBV) infection [2]. Globally, an estimated 71 million people are chronically affected with the hepatitis C virus (HCV) but only one in five knows their diagnosis [3]. The first key direction of the global health sector strategy [1] on viral hepatitis priorities includes developing a strong comprehensive information system to understand viral hepatitis epidemics and focus responses. The true public health dimensions and impact of hepatitis epidemics are poorly understood. With national and subnational data often lacking or inadequate, and hepatitis surveillance programs are weak, it is difficult to plan for focused action and prioritize the allocation of resources [1].

The absence of unique case definitions, with high sensitivity and specificity, results in underreporting. According to the Centers of Disease Control and Prevention (CDC) [4], a case definition is "a standard set of criteria for deciding whether an individual should be classified as having the health condition of interest". A good case definition is a compromise between the need for detecting all cases and being able to describe a specific disease; low sensitivity may lead to a reduced ability to control the spread of infection, while lack of specificity can overload the capacity of health services [5].

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https://doi.org/10.1016/j.jiph.2019.01.061

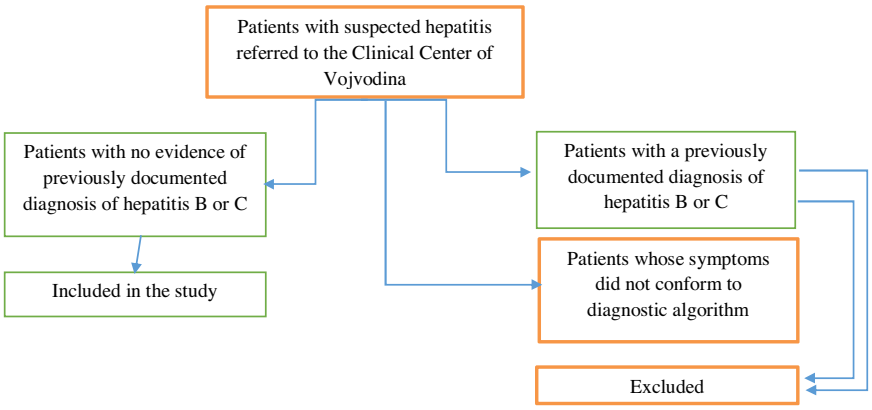

Fig. 1. Flow diagram of inclusion and exclusion criteria.

In comparison, a more specific case definition will provide a more accurate description of true cases, but at the expense of missing true cases [6]. It is a challenge to define a case definition in a way that it is sensitive and specific enough to address the aims of surveillance. However, underreporting and low sensitivity is often a cause of concern in viral hepatitis surveillance [7].

The population of Serbia is just over seven million people, and the 2015 estimated prevalence rate of hepatitis B and hepatitis C within the general population was 2.2/100, 000 and 1.04/100, 000 respectively [8]. The aim of the study was to determine and compare the sensitivity and specificity of hepatitis B and hepatitis C case definitions developed by the EC and the CDC [9–11], all in use at the time of data collection (2014/2015). The hypothesis is that only laboratory-based case definitions have satisfactory sensitivity and specificity. We used data from a small sample of patients in Serbia (which does not currently contribute data to the European surveillance network), in order to test the validity of the case definitions. Based on our knowledge, no similar research has been performed before.

Methods

This is a prospective study that used clinical, epidemiological and laboratory data from 150 patients to compare different case definitions of hepatitis B and C.

Material

Time and location of the study

The patients for the study were recruited at the Clinical Centre of Vojvodina (CCV) Clinic for Infectious Diseases, Novi Sad, Serbia. The CCV is a tertiary care institution (hospital), where both inpatients and outpatients from the South Backa district (population approximately 600,000), and on occasion, from other parts of Autonomous Province of Vojvodina (population approximately two million), are referred by general practitioners or by other clinics within the CCV. Data for the study were collected between July 2014 and October 2015.

Participants

The study included clinical, epidemiological and laboratory data for 150 patients of both sexes, all ages, residing in the Autonomous Province of Vojvodina, who were referred to the CCV Department of Infectious Diseases, during the study period, with suspected hepatitis. Patients with a previously documented diagnosis of hepatitis B or C, and patients whose symptoms did not conform to the diagnostic algorithm, were excluded (see Fig. 1 for inclusion and exclusion criteria).

To determine the sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of case definitions, patients were divided into four categories;

a) TP – 'true positive' – those with the laboratory confirmation of the presence of infection and who met the case definition criteria;
b) FP – 'false positive' – those with the laboratory confirmation of the absence of infection, and who met the case definition criteria;
c) TN – 'true negative' – those with the laboratory confirmation of the absence of infection and who did not meet the case definition criteria;
d) FN – 'false negative' – those with the laboratory confirmation of the presence of infection, but who did not meet the case definition criteria.

Method

Study design

During the study period, patients referred with a diagnosis of suspected hepatitis were tested on various hepatitis A–E markers. Hepatitis D and E are extremely rare in Europe and particularly in Serbia, with possibly one or two cases reported annually [8].

Three CCV physicians were asked to complete a report form for each patient, based on anamnestic data and clinical examination. Based on the data in the report forms, patients were matched against different hepatitis B and C case definitions in use at the time of the study (2014/2015) (see Table 1). This article presents results on hepatitis B and C case definition validity. No co-infections were observed.

Variables

Acute hepatitis B was considered to be determined by a positive nucleic acid test, with a positive anti-HBc IgM test (test of the presence of immunoglobulin M antibodies against hepatitis B core antigen) [10]. Chronic hepatitis B was considered to be determined by a positive nucleic acid test with negative anti-HBc IgM test [12]. EC 2012 [11] does not differentiate between acute and chronic, and a confirmed case includes a positive result for at least one or more of the following tests/combination of tests; anti-HBc IgM, HBsAg (hepatitis B surface antigen), HBeAg (hepatitis B "e" antigen), HBV DNA (hepatitis B virus deoxyribonucleic acid).

Active hepatitis C was considered to be determined by a positive test result for the nucleic acid acute hepatitis C (in the case of alanine transaminase (ALT), above 400 IU/mL). A past hepatitis C infection was determined by anti-HCV positive test results and negative HCV RNA (hepatitis C virus ribonucleic acid) test results.

Table 1
EC 2008, 2012 and CDC 2012 [9–11] hepatitis B and hepatitis C case definitions.

Hepatitis B	
EC 2008 acute hepatitis B case definition	The case definition of acute hepatitis B includes probable and confirmed cases (excluding possible). The definition of a probable case includes the presence of symptoms (e.g. fatigue, abdominal pain, loss of appetite, nausea and intermittent vomiting) and at least one of the three indicators (elevated body temperature, jaundice, elevated aminotransferase levels in serum), with an epidemiological link with a confirmed case of hepatitis B. The definition of a confirmed case involves the presence of symptoms (e.g. fatigue, abdominal pain, loss of appetite, nausea and intermittent vomiting) and at least one of the three indicators (elevated body temperature, jaundice, elevated serum aminotransferase levels) with a positive finding of IgM anti-HBc.
EC 2012 hepatitis B case definition	The case definition includes a confirmed case (excluding possible and probable). The definition of a confirmed case includes a positive result for at least one or more of the following tests or combinations of tests: IgM anti-HBc, HBsAg, HBeAg, HBV DNA.
CDC 2012 acute hepatitis B case definition	The case definition B includes a confirmed case (excluding possible and probable). The definition of a confirmed case considers a case that meets the clinical case definition (acute illness with a discrete beginning and any signs or symptoms consistent with acute viral hepatitis e.g. fever, malaise, anorexia, nausea, vomiting, and abdominal pain, and at least one of the following: jaundice or elevated serum ALT > 100 IU/ml), laboratory confirmation (HBsAg positive AND IgM anti-HBc positive if tested), and no previous chronic hepatitis B infection.
CDC 2012 chronic hepatitis B case definition	The definition of a chronic hepatitis B includes probable and confirmed cases (excluding possible. The definition of a probable case considers a person with a single HBsAg positive or HBV DNA positive result (including qualitative, quantitative and genotype testing) or an HBeAg positive laboratory result, and who does not meet the case definition of acute hepatitis B. The definition of a confirmed case considers a person who meets any of the criteria for laboratory diagnosis (IgM anti-HBc negative AND a positive result on one of the following tests: HBsAg, HBeAg, OR HBV DNA (including qualitative, quantitative and genotype testing) or HBsAg positive or HBV DNA test positive (including qualitative, quantitative and genotype testing) or HBeAg positive at least twice in the past 6 months (any combination of these tests carried out at intervals of 6 months is acceptable).
Hepatitis C	
EC 2008 hepatitis C case definition	The case definition of hepatitis C includes only confirmed cases (excluding possible and probable). The definition of a confirmed case involves the presence of at least one of the following two laboratory criteria: a) Detection of HCV RNA in the serum; b) Detection of hepatitis C virus-specific antibodies (anti-HCV) confirmed with other tests to determine the presence of antibodies.
EC 2012 hepatitis C case definition	a) The case definition includes a confirmed case (excluding possible and probable cases). The definition of a confirmed case includes a positive result in at least one of the following markers: b) HCV-RNA; c) HCV core Ag; d) Anti-HCV with confirmatory test (e.g. immunoblot) antibodies in people older than 18 months, but without a certificate of recovery from hepatitis C.
CDC 2012 acute hepatitis C case definition	Case definition includes a confirmed case (excluding possible and probable). The definition of a confirmed case considers: a) A case that meets the clinical case definition (acute illness with a discrete beginning and any signs or symptoms consistent with acute viral hepatitis (e.g. fever, malaise, anorexia, nausea, vomiting, and abdominal pain), and either jaundice or elevated serum alanine aminotransferase (ALT) > 400 IU/ml), or a documented negative HCV antibody laboratory test result followed within 6 months by a positive test; b) Laboratory confirmation: anti-HCV screening-test-positive, OR hepatitis C virus recombinant immunoblot assay (RIBA HCV) OR nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative or genotype testing); AND if the tests are carried out, the fulfilment of the following two criteria: absence of IgM antibodies against hepatitis A virus (IgM anti-HAV) and absence of IgM anti-HBc.), and no previous chronic hepatitis C infection.
CDC 2012 chronic hepatitis C case definition	The definition of chronic hepatitis C includes probable and confirmed cases (excluding possible). The definition of a probable case considers: a) A person that does not meet the definition for acute hepatitis C; b) Is anti-HCV positive for the enzyme immunoassay test (EIA); and c) Has increased alanine aminotransferase, but the anti-HCV EIA result has not been confirmed by an additional, more specific test or the signal to cut-off the ratio is unknown. The definition of a confirmed case considers a case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis C. Laboratory confirmation considers: a) A person who meets laboratory criteria: anti-HCV screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by CDC, OR HCV RIBA OR NAT for HCV RNA (including qualitative, quantitative or genotype testing); b) Does not meet the case definition of acute hepatitis C.

Sources: EC 2008 [9]; EC 2012 [10]; CDC 2012 [11].

For both hepatitis B and hepatitis C, the validity of the clinical and laboratory criteria (a — true positive, b — false positive, c — false negative, d — true negative) of case definition, was estimated on the basis of the formulae shown in Table 3. The values of ALT and aspartate transaminase (AST) above 100 IU (international units)/ml were considered as elevated, if they were not indicated otherwise by a case definition.

Case definitions

The following case definitions [10–12] for hepatitis B and C were tested (Table 1):

Data sources

To collect data about hepatitis B and C patients, a report form for each condition was created, which was completed by the CCV physicians. The dataset collected consisted only of data routinely collected for the purpose of surveillance and diagnosis, and consisted of the following groups of data:

a) Clinical picture (fever, headache, loss of appetite, fatigue, nausea, abdominal pain, vomiting, diarrhoea, jaundice);
b) Possible exposure to viruses — risk factors (the presence of hepatitis in the family, among partners, invasive medical and non-medical procedure, reception of blood, tissues and organs, drug use, etc.);
c) Laboratory data (results of serological testing, analysis of viral nucleic acid and analysis of serum aminotransferases).

Laboratory testing

Laboratory testing was conducted in several stages, as demonstrated in Fig. 2.

Table 2
Patient demographics by gender.

Age group (years):	Male (n = 104)			Female (n = 46)			Total (n = 150)
<20	5			3			8
20–29	19			7			26
30–39	35			10			45
40–49	25			8			33
>50	20			18			38
Median age	38			43			40
Status	Positive	Negative	Not tested	Positive	Negative	Not tested	Total (n = 150)
Tested positive for acute hepatitis A	0	104	0	0	46	0	150
Tested positive for acute hepatitis B	22	82	0	7	39	0	150
Tested positive for chronic hepatitis B	7	97	0	18	28	0	150
Tested positive for acute hepatitis C	52	52	0	20	26	0	150
Tested positive for chronic hepatitis C	4	100	0	1	45	0	150
Tested positive for hepatitis D[a]	0	29	75	0	25	21	150
Tested positive for hepatitis E	0	150	0	0	150	0	150

[a] Only patients who tested positive for hepatitis B were tested for hepatitis D.

Table 3
Numbers of patients in each group, and the sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of hepatitis B case definition and hepatitis C case definition.

Hepatitis B:

Variables	Probable case definition (acute) [9]	Confirmed case definition (acute) [9]	Confirmed case definition [10]	Confirmed case definition (acute) [11]	Probable case definition (chronic) [11]	Confirmed case definition (chronic) [11]
True positive (TP) (a)	0	23	73	23	44	44
False positive (FP) (b)	0	0	0	0	0	0
False negative (FN) (c)	29	6	0	6	6	0
True negative (TN) (d)	121	121	77	121	100	106
SN (%) a/(a + c) (95% CI)	N/A	79.3 (60.3; 92.0)	100 (95.1; 100)	79.3 (60.3; 92.0)	88 (75.7; 95.5)	100 (92.0; 100)
SP (%) d/(b + d) (95% CI)	100 (97.0; 100)	100 (97.0; 100)	100 (95.3; 100)	100 (97.0; 100)	100 (96.4; 100)	100 (96.6; 100)
PPV a/(a + b) × 100	N/A	100	100	100	100	100
NPV d/(c + d) × 100	80.7	95.3	100	95.3	94.3	100

Hepatitis C:

Variables	Confirmed case definition [9]	Confirmed case definition [10]	Confirmed case definition (acute) [11]	Probable case definition (chronic) [11]	Confirmed case definition (chronic) [11]
True positive (TP) (a)	72	72	5	25	67
False positive (FP) (b)	0	0	0	0	0
False negative (FN) (c)	0	0	0	43	0
True negative (TN) (d)	78	78	145	82	83
SN (%) a/(a + c) (95% CI)	100 (95.0; 100)	100 (95.0; 100)	100 (47.8; 100)	36.8 (25.4; 49.3)	100 (94.6; 100)
SP (%) d/(b + d) (95% CI)	100 (95.4; 100)	100 (95.4; 100)	100 (97.5; 100)	100 (95.6; 100)	100 (95.6; 100)
PPV a/(a + b) × 100	100	100	N/A	100	100
NPV d/(c + d) × 100	100	72	N/A	65.6	100

Note: N/A = not applicable.

Statistical analysis

The sample size was estimated as an expected annual number of patients diagnosed with hepatitis B and C in CCV, based on average annual number of patients diagnosed with hepatitis B and C at the CCV in previous years.

Statistical analyses were performed using the software package, IBM® SPSS® Statistics 21 (the first author had the licence). During the statistical analyses of the data, the sensitivity and specificity of case definition were determined in relation to the results of laboratory testing, in addition to frequencies, percentages, specific incidence, and 95% confidence intervals (CI). As the distribution of the data was normal, comparison and determination of the existence of statistical significance for binary variables sensitivity and specificity were performed using the χ^2 test and Fisher's test, Anova, and Kruskal–Wallis text.

Ethical approval

The study was approved by the Board of Ethics of the University of Novi Sad, Faculty of Medicine and by the Board of Ethics of the Clinical Centre of Vojvodina. As the study included only patients' that are data mandatory collected according to the Law on population protection against communicable diseases [12], the two boards of ethics decided there was no need for patients' consent for this research.

Results

Demographic characteristics of the respondents

The study included 104 males and 46 females. The youngest participant was 15 years old and the oldest 72 years. The median age was 40 years. The structure of patients, identified a signifi-

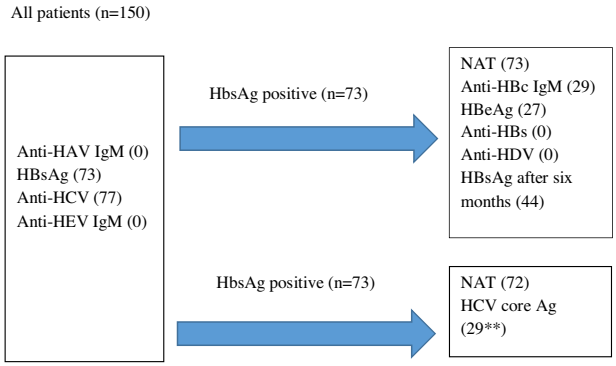

Fig. 2. Laboratory testing (positive)*.
*Serological markers testing was done withVIDAS® Hepatitis panel on devices mini VIDAS® — bioMérieux SA, Lyon; nucleic acid tests using the COBAS® TaqMan HBV Test v2.0 on the device COBAS® AmpliPrep/COBAS® TaqMan System v2.0); nucleic acid tests using the COBAS® AmpliPrep/COBAS® ; TaqMan® HCV Quantitative test on the device COBAS® AmpliPrep/COBAS® TaqMan System v2.0).
**Due to limited financial resources, test for the presence of HCV core Ag was conducted on 50 patients (30 anti-HCV positive and 20 anti-HBsAg positive, for the purpose of test validation).

cantly higher proportion of respondents aged 20–49 years (17% in age group 20–29, 31% in age group 30–39 and 23% in age group 40–49), ($\chi 2 = 17.724$, df = 5, $p < 0.01$) compared to other age groups (see Table 2).

The results for SN, SP, and NPV for the different hepatitis B and hepatitis C case definitions are outlined in Table 3, and described below.

Case definitions

Acute hepatitis B (EC 2008) [9]

As an epidemiological link was not reported by any of the patients, the sensitivity and PPV of case definition for probable case could not be calculated. Six patients who had had laboratory confirmed acute hepatitis B did not meet the case definition criteria, because they had not fulfilled the clinical criteria, the presence of which is required.

Hepatitis B (EC 2012) [10]

All patients with hepatitis B (54 out of 150) met the definition of a confirmed case.

Acute hepatitis B (CDC 2012) [11]

As with the EC definition of a confirmed case for both acute and chronic hepatitis B, which in addition includes laboratory and clinical criteria, and within the CDC case definitions, false negative results appear — those people who have laboratory confirmed acute hepatitis B (defined as positive anti-HBc IgM positive finding of HBV DNA), which is reflected by the reduced sensitivity of the case definition, with maximum specificity.

Chronic hepatitis B (CDC 2012) [11]

As the probable case definition includes those who meet the laboratory criteria and who do not meet the case definition of acute hepatitis B (because of the absence of clinical criteria) and thus they are classified as false negative, the use of the definition of a probable case may lead to false positive cases. For all patients for whom some laboratory parameters were positive (and) after six months, the maximal case definitions sensitivity and specificity were confirmed.

Hepatitis C (EC 2008) [9]

This case definition includes confirmed cases only. All patients with the laboratory confirmed presence of HCV infection have fulfilled the case definition criteria and sensitivity and specificity are maximal. As the PCR could not be done in the majority of subjects who were anti-HCV negative, but diagnosed with hepatitis B infection, data on sensitivity and specificity should be interpreted with caution. However, it could be expected that the probability of acute co-infection with hepatitis B and C in these patients was extremely small.

Hepatitis C (EC 2012) [10]

This case definition also includes confirmed cases only. All patients with the laboratory confirmed presence of HCV infection have fulfilled the case definition criteria, and sensitivity, specificity, PPV and NPV are maximal. As the PCR could not be done in the majority of subjects who were anti-HCV negative, but diagnosed with hepatitis B infection, data on sensitivity and specificity should be interpreted with caution. However, it could be expected that the probability of acute co-infection with hepatitis B and C in these patients was extremely small.

Acute hepatitis C (CDC 2012) [11]

Casedefinitions for possible and probable cases were not applicable. Five patients fulfilled the criteria for acute hepatitis C, with maximal sensitivity, specificity, PPV and NPV.

Chronic hepatitis C (CDC 2012) [11]

This is the only case definition that was applicable to probable cases, however, a very low sensitivity (36.8%) with maximal specificity was found. While the positive predictive value was maximal, the negative predictive value was 65.6% and negative likelihood ratio was 0.63.

For the laboratory confirmed case definitions, maximal sensitivity, specificity, PPV and NPV were found.

Discussion

Our study found that case definitions which rely on clinical signs and symptoms (EC 2008 case definition for acute hepatitis B, CDC 2012 case definition for acute hepatitis B, and CDC 2012 case definition for probable case of chronic hepatitis B) have low sensitivity. Case definitions which rely on laboratory confirmation only (EC 2008 case definition for hepatitis C, EC 2012 case definition and CDC 2012 case definition for confirmed cases) have maximal (100%) sensitivity, affirming in that way our hypothesis. Likelihood ratios indicate the extent to which the results of the test change the probability of diagnosis before the test. In our study, likelihood ratios showed that the case definition does not significantly affect the change in the probability of diagnosis of the disease.

In 2016, WHO proposed case definitions for acute and chronic hepatitis B [13]. Only case definitions for confirmed cases have been proposed, which is in line with our finding. It seems that case definitions for probable cases of hepatitis B (clinical manifestations with an epidemiological link) should be used in hepatitis B outbreaks only, when laboratory confirmation is not available (e.g. retrospective investigation). The WHO definition of acute hepatitis B is similar to EC's 2008 case definition (clinical manifestations plus detection of anti-HBc IgM), while the case definition of chronic hepatitis B considers a person not meeting the case definition for acute hepatitis plus detection of HBsAg [13].

CDC recently updated its case definition for acute hepatitis C [14]. The significant threshold for ALT has been decreased to 200 IU/L, and laboratory criteria include a positive anti-HCV test result or nucleic acid test (NAT) for HCV RNA, or a positive test indicating presence of hepatitis C viral antigen(s) (instead of a positive

RIBA test result as it was defined by 2012 case definition). WHO case definition for acute hepatitis C from 2016 defines acute hepatitis C as a case with clinical criteria and one of three laboratory criteria: detectable HCV RNA and negative for anti-HCV antibodies or seroconversion to anti-HCV antibodies or a positive result for anti-HCV AND negative for IgM anti-HBc, IgM, anti-HAV and IgM anti-HEV [13].

The assumption that the differences between the clinical case definition and the formal set of criteria intended for the purpose of epidemiological surveillance can be huge, and almost questions the appropriateness of control, confirmed by a recent study published in Massachusetts [15]. Out of 183 reported cases of acute hepatitis C reported for surveillance classification, with 43 of these investigated, only one reported case met the case definition criteria. The complete fulfilment of the criteria of the CDC case definition was confirmed in only one person. As reasons for inadequate control of the disease, the authors of this study stated "incomplete reporting by doctors of clinically problematic case definitions, limited diagnostic testing and incomplete collection and processing of data collected despite the existence of an electronic reporting system" [15,p.2]. An Australian survey found a distinct heterogeneity of the case definition of acute hepatitis C, mainly due to the width of the period of anti-HCV seroconversion and ALT threshold level [16].

In our study, the sensitivity and the specificity of laboratory criteria were maximal, as well as their positive and negative predictive value, and showed that the case definition does not significantly affect the change in the probability of diagnosis of the disease. Epidemiological studies conducted for the purpose of surveillance are mainly based on an extended 'window period' (anti-HCV conversion), in order to increase the sensitivity of the case definition, while clinical studies aim to study the natural course of the disease based on increasing the specificity and shortening the 'window period' [17].

The limitations of our study are reflected in the inability to detect early infection when the patient is in the 'window period', the lack of a single laboratory test as a 'gold standard' (e.g. to distinguish between the acute and the chronic hepatitis B it is necessary to know the results of the IgM anti-HBc and HBV DNA), and consequently, artificially matching confirmation of the diagnosis ('gold standard') with laboratory case definition criteria. Therefore, data on the sensitivity and specificity of a certain confirmed case definition should be interpreted with caution. The significant difference in sensitivity and specificity between the case definitions which include, and those which do not include, clinical and epidemiological criteria, in addition to the laboratory criteria, should be interpreted in accordance with the above. An additional constraint was the limited number of patients (n = 73) who were tested for HBV DNA. Based on this limitation, a patient was considered a hepatitis B case based on a negative HBsAg and IgM anti-HBc finding. Similarly, few patients (n = 77) were tested for HCV RNA.

Conclusion

Syndromic case definitions show low sensitivity and are of limited use. They highlight the importance of laboratory diagnostics (offering maximal sensitivity and specificity, and high positive and negative predictive values), as well as the need for universal case definitions, for confirmed cases only.

In order to improve the system of epidemiological surveillance of hepatitis B and hepatitis C, further research is needed, involving a larger number of respondents, from the general population, in order to determine sensitivity and specificity of the case definition based on confirmed laboratory criteria. A degree of standardisation relating to case definitions would facilitate a more uniform evaluation of viral hepatitis prevention and management strategies.

Funding

No external financial support was used. The costs for the tests not routinely performed at the CCV were covered by the first author.

Competing interests

None declared.

Ethical approval

Not required.

Acknowledgements

The authors want to thank to Ms. Claire McLellan and Dr. Nicole Vidal, Institute for Global Health and Development, Queen Margaret University Edinburgh, for language and grammar editing.

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