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Acute hepatitis B (England): annual report for 2016

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Introduction

Hepatitis B is a blood borne infection of the liver caused by the hepatitis B virus (HBV). The virus can provoke an acute illness characterised by nausea, malaise, abdominal pain, and jaundice but can also produce a chronic persistent infection that is associated with an increased risk for chronic liver disease and hepatocellular carcinoma. Transmission is by parenteral exposure to infected blood and body fluids contaminated by blood, most often through sexual contact, blood-to-blood contact and perinatal transmission from mother to child. HBV infection can be prevented by immunisation and in the UK immunisation is recommended for individuals at high risk of exposure to the virus e.g. people who inject drugs (PWID), healthcare workers and household contacts of people who are acutely and chronically infected with hepatitis B. Immediate post-exposure immunisation is used to prevent infection, especially in babies born to infected mothers or following needle-stick injuries [1]. In autumn 2017, the UK also introduced hepatitis B containing hexavalent vaccine into the routine infant immunisation programme [2].

Surveillance of acute hepatitis B is essential to target prevention and control activities such as the selective immunisation programme. Public Health England, formerly the Health Protection Agency (HPA), implemented national surveillance standards [3] for hepatitis B in 2007 which provided the framework for more consistent reporting of cases from PHE Centres. Available data on confirmed acute infections reported from laboratories can then be used to augment the epidemiological data collected from the local centres. The first report was published in 2008 and this current report provides an update and presents acute hepatitis B surveillance data for 2016. The section titled, “Reference laboratory confirmation and genotyping of acute hepatitis B infection” summarises molecular characterisation of samples captured through HPZone in the “Acute Hep B” context with samples forwarded and tested at the Viral Reference Department (VRD), Colindale.

Methods

The surveillance definition for acute hepatitis B [3, 4] is:
“HBsAg positive *and* anti-HBc IgM positive *and* abnormal liver function tests with a pattern consistent with acute viral hepatitis.”

As information on liver function is usually not available to PHE, for the purpose of this analysis:

- cases classified as acute viral hepatitis B by the local PHE Centre or the laboratory and/or with a documented positive anti-HBc IgM were classified as acute cases;
- cases classified as acute viral hepatitis B by the PHE Centre but without anti-HBc IgM test results, or not classified but with a positive anti-HBc IgM reported were assumed to be probable acute hepatitis B cases;
- cases classified as acute by the PHE Centre but with contradictory evidence e.g. positive hepatitis serology results dated before July 2012 were reclassified as chronic infections;
- cases classified as chronic infections or those not classified where anti-HBc IgM was negative or equivocal were assumed to be chronic infections;

PHE Centre cases with a date entered from 1 January 2016 to 31 December 2016 were extracted from HPZone and matched to a laboratory dataset using Microsoft Access and algorithms comparing combinations of the following variables: surname, first name, date of birth, sex, clinic number and NHS number. The laboratory database contained all confirmed hepatitis B infections reported to PHE by laboratories in England and Wales (SGSS). A final reconciled dataset included cases classified as acute or probable acute and reported from the PHE Centre and/or from laboratories around the country to SGSS. After follow up with the clinician and/or the patient, PHE Centre staff assigned a probable route of exposure and collected information on other possible exposure routes. For the analysis, where the probable route of exposure had not been assigned due to more than one exposure, the most likely route was assigned hierarchically (people who inject drugs, followed by sex between men, then heterosexual exposure, etc.).

Results

PHE Centres reported 5,242 hepatitis B cases from 1 January to 31 December 2016 to the PHE Immunisation, Hepatitis and Blood Safety Department. The matching and classification exercise resulted in 286 of these being confirmed as acute and 43 re-classified as probable acute cases with the remainder classified as chronic or excluded.

A total of 11,901 confirmed hepatitis B infections were reported from laboratories to SGSS in the same period, 303 (2.5%) of which were classified as acute cases, 24 (0.2%) as probable acute cases. The remainder were classified as chronic.

After the two databases were linked and reconciled, a total of 453 acute or probable acute cases of hepatitis B were reported for England in 2016. This gives an annual incidence of 0.82 per 100,000 populations lower than the incidence of 0.83 per 100,000 population reported for 2015.

London is still the region with the highest incidence (1.70 per 100,000) and this has increased from the previous year (1.53 per 100,000). The highest increase in incidence was reported from North West region (from 0.64 to 1.02 per 100,000 in 2015 and 2016 respectively) and North East (from 0.34 to 0.68 per 100,000). The largest decrease was reported from East Midlands (from 1.07 to 0.70 per 100,000 in 2015 and 2016 respectively) and West Midlands (from 0.85 to 0.50 per 100,000 in 2015 and 2016 respectively).

In the remaining regions incidence was similar or slightly declined from last year (table 1) except for London where there was an increase. There continues to be regional variation in the contribution of the different data sources to the overall total, although the overlap between sources has continued to improve suggesting that completeness of reporting by laboratories and local clinicians has also improved.

As in previous years, where known the majority of cases were in men (66.2%) who had an overall incidence of 1.09 per 100,000 – a decrease from 1.17 per 100,000 in 2015 compared to a continuing decline from the previous year [3]. The corresponding incidence in women in 2016 was 0.55 per 100,000 an increase from 0.49 per 100,000 in the previous year. Men aged 25-34 years had the highest incidence of acute hepatitis B in 2016 at 1.92 per 100,000.

Only 80 cases (17.7%) of the total acute or probable acute hepatitis B cases had their ethnicity recorded; a lower proportion than the previous year. Seventy nine percent of the cases were white (an increase from 66% in 2015), followed by Black or Black British (12.5%) and Asian or Asian British (8.75%).

Of the total 453 acute and probable acute cases of hepatitis B, 164 (36%) had associated exposure information recorded (with the most probable route of acquisition assigned by the PHE Centre). A higher proportion (56% 256/457) had exposure information available in 2015. As in previous years where known the commonest reported risk attributed was heterosexual exposure, implicated as the probable route of exposure in 106 (64.6%), compared to 56.6% in this category in 2015 (n=145). Cases attributed to sex between men were reported in 23 (14 %); a similar proportion to the 40 (15.6%) reported in 2015. Twelve cases (7.3%) with known exposure were attributed to PWID (an increase from 3.5% in the previous year).

Where known, 9 (5.5 %) cases had health care related exposures (including surgery, dental treatment, and other hospital exposure) – a decrease compared to the 21 (8.2%) cases assigned to medical risk factors last year. Skin piercing, tattooing and acupuncture combined were listed as probable exposures for four cases (2.4%, 4/164).

Discussion

In 2016, reporting of acute cases of hepatitis B from PHE Centres has continued to exceed the number reported from laboratories but the proportion of cases reported by both PHE Centres and laboratory systems is high at 43.7% (198/453), compared to 59.1% (270/457) of cases reported in 2015. This slight decrease in overlap may be due to the introduction a new database to process the SGSS laboratory reporting system data.

There was nonetheless an overall improved matching over the years that could be explained given the introduction of statutory laboratory reporting in October 2010 and the continued decline in the proportion of cases of unknown status reported from laboratories. Combining data from both sources does minimise under ascertainment and improve the completeness of associated data for analysis. Interpretation of trends should be made with caution, but based on this combined data, the incidence of acute hepatitis B remains low. Given the improved quality and completeness of data provided in 2015/2016, it is likely that there has been a continued gradual decline in incidence since 2008 which has become more apparent in the more recent years.

It is known that anti-HBc IgM, normally a marker of acute infection, may be detected during flares in chronic infections. To minimise misclassification, matching to historical laboratory reports can identify those chronic infections detected previously. However, there is still likely to be some misclassification of chronic cases as acute infections in both datasets. Given the large number of chronic cases diagnosed each year, even a small proportion of cases

misclassified as acute can substantially increase the estimated incidence of acute hepatitis B, and confuse the attribution of exposures. Further testing using anti-HBc avidity is now being offered at PHE Colindale, to enable better distinction between acute and chronic infection. Local laboratories can send samples from IgM positive cases to the national virus reference laboratory where both genotyping and avidity testing will be undertaken free of charge [6].

Risk factor data were available in 36% of cases. The interpretation of these data is difficult because in many instances, more than one possible exposure is listed and a probable exposure had not been assigned by the local HPT. Despite this, the data suggest that the number of cases in PWID has remained low in 2016. The overall low incidence in this group is supported by the 2016 Unlinked Anonymous Monitoring Survey of people who Inject Drugs in contact with drug services which showed that anti-HBc prevalence has remained low and self-reported uptake of hepatitis B vaccine has remained high since 2009, particularly in recent initiates, and HBsAg prevalence among anti-HBc positives has remained very low [7]. Improved reporting of risk factors associated with HBV acquisition will enable a more comprehensive interpretation of surveillance trends and appropriate response to clusters.

The incidence of acute hepatitis B continues to remain higher in males than females. This excess of male cases is partly explained by cases in men who have sex with men (MSM); the number of cases with this exposure reported has remained high again this year, following a large increase in 2010. Such cases are more likely to attend GUM clinics, reinforcing the important role of GUM clinics in providing opportunistic hepatitis B immunisation to MSM and individuals with multiple sexual partners. The joint PHE and British Association of Sexual Health and HIV (BASHH) standard form for GUM clinics to report acute hepatitis to their local Health Protection Team continues to improve the reporting of cases diagnosed in this setting [8].

In addition, following recent clusters of acute hepatitis B in men who did not disclose MSM activity initially [9], an enhanced surveillance questionnaire for acute hepatitis B cases was developed in 2016 to support HPTs in obtaining risk factor information on cases with undisclosed risk factors, particularly during outbreaks, to inform and target control measures.

Table 1. Acute or probable acute hepatitis B cases by region and source of report, 2016 (incidence 2008-2014 – mid 2013 population, incidence 2015 – mid-2015 population and incidence 2016 – mid-2016 population ONS [5])

REGION	HPU	Laboratory	BOTH	TOTAL	**Incidence of reported acute hepatitis B per 100,000 in 2016**	Incidence of reported acute hepatitis B per 100,000 in 2015	Incidence of reported acute hepatitis B per 100,000 in 2014	Incidence of reported acute hepatitis B per 100,000 in 2013	Incidence of reported acute hepatitis B per 100,000 in 2012	Incidence of reported acute hepatitis B per 100,000 in 2011	Incidence of reported acute hepatitis B per 100,000 in 2010	Incidence of reported acute hepatitis B per 100,000 in 2009
EAST MIDLANDS	18	2	13	33	**0.70**	1.07	0.41	0.35	0.77	0.76	0.74	0.85
EAST OF ENGLAND	15	3	20	38	**0.62**	0.76	0.89	0.81	0.89	1.08	0.78	0.85
LONDON	23	77	49	149	**1.70**	1.53	1.52	1.22	2.02	2.06	1.82	1.8
NORTH EAST	5	0	13	18	**0.68**	0.34	0.84	0.65	0.46	0.54	0.54	1.28
NORTH WEST	29	16	29	74	**1.02**	0.64	0.82	0.87	0.61	0.99	0.96	1.64
SOUTH EAST	13	10	21	44	**0.49**	0.69	0.71	0.67	0.84	0.96	0.84	1.03
SOUTH WEST	11	5	13	29	**0.53**	0.49	1.08	0.63	1.40	1.16	1.05	0.78
WEST MIDLANDS	7	0	22	29	**0.50**	0.85	0.78	0.55	0.98	0.90	0.66	0.74
YORKS AND HUMBER	10	11	18	39	**0.72**	0.65	0.82	0.82	0.83	1.06	0.97	1.05
NATIONAL	**131**	**124**	**198**	**453**	**0.82**	**0.83**	**0.91**	**0.77**	**1.04**	**1.13**	**0.99**	**1.15**

Table 2. Age and sex breakdown of acute or probable acute hepatitis B reports, 2016 (incidence 2008-2014 – mid 2013 population, incidence 2015 – mid-2015 population and 2016 – mid-2016 population ONS [5])

	Female		Male		NK		TOTAL	
Age group	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population
LT15	1	0.02	5	0.10		–	6	0.06
15-24	34	1.04	26	0.75	1	–	61	0.91
25-34	29	0.77	73	1.92		–	102	1.35
35-44	33	0.93	58	1.64		–	91	1.28
45-54	28	0.71	66	1.72	1	–	95	1.22
55-64	10	0.31	32	1.03		–	42	0.67
GE65	17	0.32	38	0.85		–	55	0.56
NK	1	0.00	0	–		–	1	0.00
Total	153	0.55	298	1.09	2	–	453	0.82

Reference laboratory confirmation and genotyping of acute hepatitis B infection

Background

In 2016, PHE's Blood Borne Virus Unit (BBVU) in the Virus Reference Department (VRD) reintroduced anti-HB core avidity testing alongside existing genotyping of samples of acute hepatitis B free of charge. Hospital microbiology/virology departments are requested to send samples to Colindale for confirmation, avidity testing and genotyping as part of the national enhanced surveillance of acute hepatitis B [10].

Following clusters of acute hepatitis B in 2016, an HPZone context "**Acute Hepatitis B"** has been added**.** Assignment of cases to the context allows Colindale to rapidly identify cases and request samples directly from laboratories for molecular characterisation at VRD, Colindale.

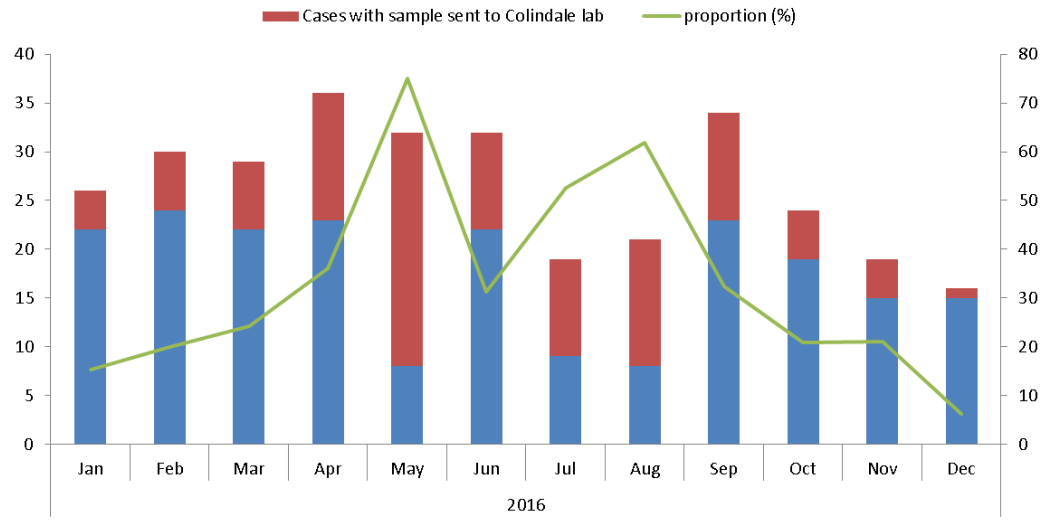
Methods

Acute hepatitis B cases entered on HPZone between 1 January, 2016, and 31 December, 2016, were extracted from the HPZone. The cases with the Acute Hepatitis B context were matched to laboratory testing data from the Virus Reference Department (VRD) using Microsoft Access algorithms comparing combinations of surname, first name, date of birth, sex and NHS number.

Results

In 2016, 356 cases of acute hepatitis B were reported onto HPZone across England (as confirmed, probable and possible)*; 89.9% (320/356) of the cases had the acute hepatitis B context added. 38.1% (122/320) of cases with an acute hepatitis B context added in 2016 had samples forwarded to VRD, Colindale.

Figure 1: Acute hepatitis B cases on HPZone in 2016 with acute hepatitis B context added with samples forwarded to VRD, Colindale by month



***** Classified according to HPZone case definitions

Confirmation and genotyping of acute hepatitis B infection

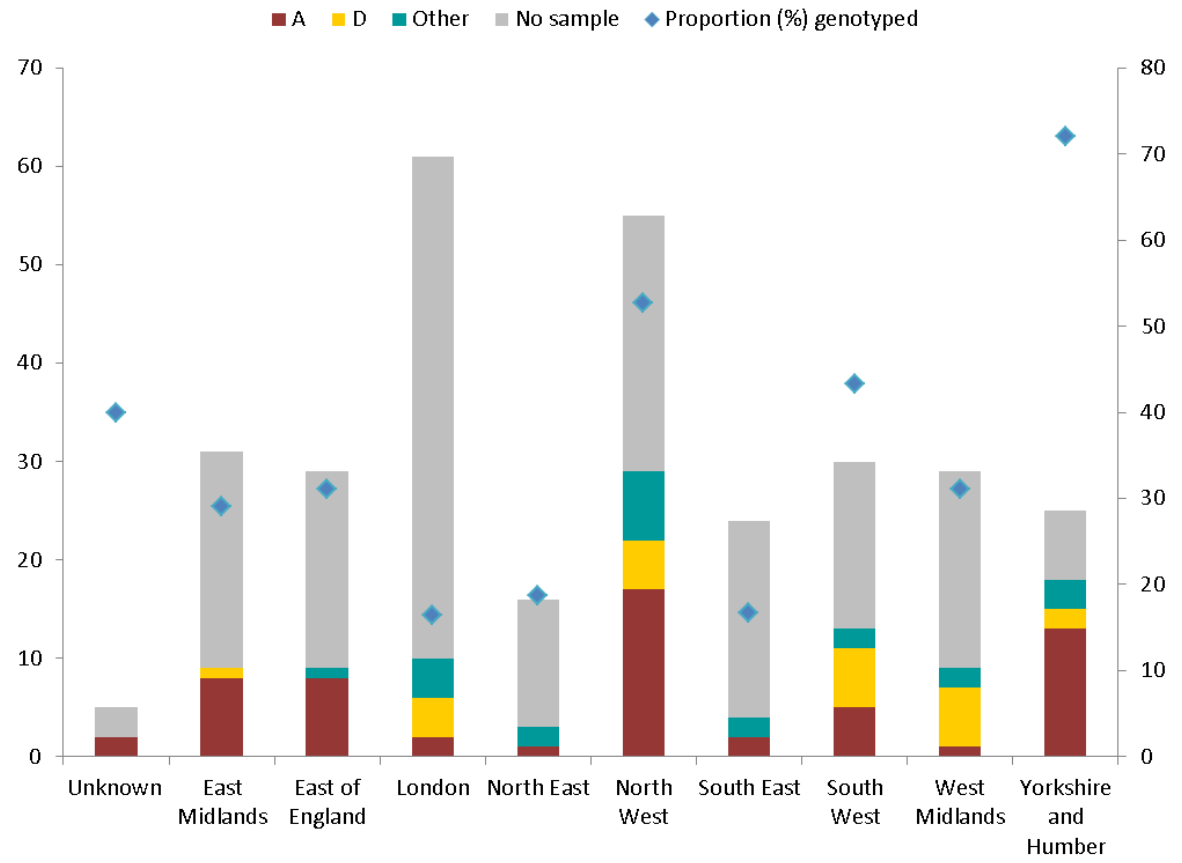
In 2016, a total of 122 samples were received at VRD, Colindale for avidity testing and molecular characterisation and matched to the HPZone cases. Avidity testing was complete on 110 samples and confirmed the acute hepatitis B diagnosis in 70% (77/110) of patients. Ten percent (12/110) of samples displayed a high avidity indicating that they were unlikely to be a recent HBV infection with the remaining 19% (20/110) samples assigned a 'grey' result where an avidity result could not be assigned with confidence.

Genotype data was available for 33.1% (106/320) of acute hepatitis B cases with an HPZone "Acute Hepatitis B" context. Genotyping classified 55% of these cases (59/106) as genotype A (54 subtype A2 and 5 subtypes A1) and 22.6% as genotype D. Table 1 shows the geographic distribution of genotypes, and figure 1 shows the proportion of samples sent to VRD.

Table 1. Genotype distribution of acute hepatitis B cases tested at VRD in 2016

Genotype	Cases	Proportion of cases
A	59	55.6%
B	8	7.5%
C	9	8.5%
D	24	22.6%
E	3	2.8%
F	2	1.9%
G	1	0.9%
Total	106	

Figure 3. Genotype distribution of acute hepatitis B cases with HPZone context, by region, 2016



Discussion

Publication of molecular analyses provides insight into the current hepatitis B genotypes circulating in England, although interpretation is limited by the proportion of samples submitted to VRD. Timely assignment of cases to the HPZone context and improved submission of samples for molecular characterisation will allow for a more comprehensive monitoring of acute hepatitis B infection in England.

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Health Protection Report is a national public health bulletin for England and Wales, published by Public Health England. It is PHE's principal channel for the dissemination of laboratory data relating to pathogens and infections/communicable diseases of public health significance and of reports on outbreaks, incidents and ongoing investigations.

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