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Uptake of Hepatitis B Treatment Eligibility Tests Among Hepatitis B Patients; The Case of Yumbe Regional Referral Hospital, Uganda.

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Abstract

Background: Despite hepatitis B virus infection being a vaccine preventable liver disease, 257 million people are estimated to be chronically infected globally making it one of the commonest infections, causing more than 820,000 deaths annually worldwide. Uganda is one of the SSA that continues to be highly endemic with a prevalence of 4.3%, associated with poor clinical management of those infected.

Objectives: Assess factors associated with the uptake of recommended HBV treatment eligibility tests among hepatitis B Virus patients at Yumbe Regional Referral Hospital.

Methods: Data was collected using both quantitative and qualitative approaches. Chi square and modified Poisson regression analyses were undertaken to determine association of factors. 01 Focus Group Discussion and 04 Key Informant interviews were conducted to explore factors affecting the provision of recommended hepatitis B treatment eligibility tests. Data was analyzed using inductive thematic analysis.

Results: 1.01% of patients took all 4 tests and 26.6% received at least one test. Complete Blood Count was mostly consumed, 38.2% while Ultra Sound Scan was the least -7%, 7.5% patients were screened for HIV with 33.3% being HIV/HBV coinfected. 61.3% patients did not take any main test and 31.2% had a main test taken. Only 7.5% had both main tests. Uptake of main tests was associated with timing of tests ($\chi 2$ = 94.9, P< 0.000), HIV/HBV coinfection ($\chi 2$ = 20.46, P<0.000), duration in care, ($\chi 2$=68.9, P<0.000), average distance to hospital ($\chi 2$ = 15.5, P<0.017). Timing of tests was the only factor statistically associated with uptake of main recommended tests (PR = 0.44, 95% CI 0.210 – 0.92). Facilitators for provision of HBV tests included availability of commodities, HCWs' knowledge of the treatment guidelines and good infrastructure while barriers were insufficient human resource, commodity stock outs and language barrier.

Conclusion: There was poor uptake of recommended tests by HBV patients at YRRH. Health Workers should endeavor to provide all recommended tests before HBV treatment initiation.

Keywords: Uptake, Hepatitis B, Treatment Eligibility, Recommended Treatment tests.

Introduction

Background

Hepatitis B infection remains a major public health challenge globally. World Health Organization (WHO) estimates that 257 million people were living with chronic hepatitis B infection in 2019 with 1.5 million new infections yearly **[1]**. WHO also estimated 820,000 deaths to have resulted from hepatitis B virus (HBV) in 2019 with majority being caused by cirrhosis and hepatocellular carcinoma (HCC) **[1,2]**. Sub -Saharan African (SSA) nations carry a significant portion of hepatitis B virus (HBV) burden on the African continent with a sero-prevalence of 6.1% **[3,4]**. Majority of those infected remain undiagnosed, untreated and poorly managed **[5]** due to limited access to accurate, timely and appropriate diagnostic services, and other health system associated factors. Uganda continues to be highly endemic with HBV, with transmission occurring both in childhood and adulthood with varying national and regional prevalence rates. Results from the 2005 national sero-survey showed a HBsAg prevalence rate of 10.3% among adults **[6]** while it stood at 4.3% in the 2016 Uganda Population – based HIV Impact Assessment (UPHIA) survey **[7]**. From the same survey, varying regional HBV prevalence rates were reported with the highest being in Northern region; mid North had at 4.6%, North East had 4.4% while 3.8% was

reported in West Nile five times that reported in South West. Of the 3.8% regional prevalence, the Yumbe district contributed 6.3% **[8]**.

Viral hepatitis is an infection that causes liver inflammation and damage **[9]**. In highly endemic areas, HBV is mostly transmitted from mother to child at birth or through horizontal transmission by percutaneous and sexual exposure, as well as by close person-to-person contact presumably by open cuts and sores, especially among children. However, chronic infection development is common in infants infected by their mothers or before the age of 5 years, contributing to about 95% of chronic cases and less than 5% for adults infected after 20 years of age **[1,10]**. This, therefore, justifies the need for strengthening infant and childhood vaccination. Furthermore, its transmission is similar to that of Human Immunodeficiency Virus (HIV), therefore, making coinfection with HIV and HBV usual **[11]**. It is reported that about 1% of those infected with HBV (2.7 million people) are also infected with HIV, resulting in a 7.4% global prevalence of HIV/HBV coinfection **[1]**.

Hepatitis B surface Antigen (HBsAg) testing, using WHO recommended Rapid Diagnostic Test (RDTs) strips is the entry point to prevention, care and treatment services- the presence of this antigen means that the person is infected. The HBsAg positively tested patients are linked into care. The Uganda HBV treatment and management guidelines **[12]**, however, do recommend that laboratory tests (Complete Blood Count (CBC), Liver Functional Tests (LFTs), HIV serology, HBV viral load if available and Abdominal ultrasound scan) are used to evaluate these positive patients for treatment eligibility. CBC and LFTs are main recommended tests since they aid Aminotransferase Platelet Ratio Index (APRI) score calculation by the health care providers. Patients whose APRI score is greater than 2 are initiated on HBV treatment while those with a value less than 2 are differed. These tests are repeated every 6 months for monitoring of disease progress.

Majority of those newly infected do not experience any symptoms, however, some have acute illness with symptoms such as yellowing of eyes and skin, extreme fatigue, nausea, dark urine, and abdominal pain. Acute liver failure, which sometimes leads to death is experienced by people with acute infection. HBV infection is the leading cause of chronic hepatitis, liver cirrhosis and HCC worldwide as long term complications, leading to morbidity and mortality **[1,13]**. Many people with HBV are unaware that they carry the infection. This is further complicated by the fact that one cannot clinically differentiate hepatitis B from hepatitis caused by other viral agents, thus justifying laboratory confirmation and the use of several recommended blood tests to monitor those infected as well as distinguish acute and chronic hepatitis B (CHB) infections **[1]**. Those that serologically test negative are recommended to get vaccinated. Those who are chronically infected, only a small proportion receives routine, scheduled follow-up to monitor their disease status and progression **[6]** prior to and during treatment.

Before HBV treatment initiation, patients are assessed to determine the extent of liver disease and also rule out HIV/HBV coinfection. The HBV management guidelines **[9,14]** recommend that at least monitoring of serum alanine transferase (ALT)- a liver functional test (LFT) and HBV deoxyribonucleic acid (DNA) levels (i.e., HBV DNA threshold above >20,000 IU/mL) is done for patients who tested positive prior to treatment initiation and during treatment. A complete blood count (CBC) is equally done to aid calculation of APRI while HIV test helps rule out HBV/HIV coinfection. The APRI score is the recommended blood based non-invasive test given its simplicity and availability **[15]**. In addition, a liver ultrasound scan (USS) is done to check for liver cancer or cirrhosis as tumors, abscesses or cysts of the liver may be seen on a liver scan. These tests are recommended annually to determine any persistent abnormality among the above parameters to aid timely identification, diagnosis and management of patients whose disease condition is progressing to cirrhosis **[9,14,16,17]**. All children, adolescents and adults with chronic hepatitis B who have clinical evidence of cirrhosis, all HIV/HBV co-infected patients, all patients with APRI score < 2 but have persistent elevated ALT over a period of 6-12 months and HBV DNA > 20,000 IU/Ml are eligible for treatment **[12]**.

The same guidelines recommend frequent monitoring of patients already with fluctuating raised ALT or HBV DNA levels (between 2,000 IU/mL and 20,000IU/mL) since they are already at increased risk of progression to active disease. However, access to these tests remains limited and there is longer waiting time when accessed especially in SSA **[18]**. It should, however, be noted that literature on the uptake of these recommended HBV diagnostic tests remains scarce in Uganda despite the national roll out of HBV treatment programs and its integration in all district general and regionalreferral hospitals (Ministry of Health, 2019).

Vaccinating older children and adults was found to have negligible sustained effects on HBV rates in a population especially in Africa, however, test and treat of HBV predicted to have a substantial impact. This, therefore, justifies diverting resources to improving diagnosis and timely treatment of the existing infections **[19]**.

A good number of studies have been conducted in Africa, and specifically Uganda, on the uptake of other hepatitis B services specifically screening and vaccination **[20-25]**. However, limited literature remains available on the uptake of the HBV recommended treatment eligibility tests (CBC, LFTS, HIV and USS) in rural settings, as well as factors affecting their uptake as no study has been conducted in Uganda and specifically Yumbe.

In May 2016, WHO adopted a strategy for the elimination of viral hepatitis as a public threat by 2030 with ambitious targets being set; a 90% reduction in new cases of chronic HBV and HCV, and a 65% reduction in mortality due to HBV and HCV infection, both of which rely on 80% of treatment of eligible individuals with chronic HBV and HCV infections being appropriately treated globally **[9,26]**. In

order to strengthen measures to improve access to vaccination and treatment, more attention needs to be paid towards access to affordable and high-quality diagnostics if testing must reach the levels needed to achieve elimination goals **[27]**. This requires decentralization of simplified models of care by removing requirements of specialized prescribing to reach those in need alongside the sustained efforts to tackle stigma and discrimination associated with hepatitis B disease.

To achieve these high and ambitious targets, several interventions have been implemented by the Ugandan government including; the vaccination program among children since 2002 **[28]**, the development and provision of HBV testing and treatment guidelines as well as strategic plans **[12]**, mass screening and vaccination done in 2018 in the highly endemic regions of Northern, West Nile, Karamoja and Teso **[29]** and the decentralization and integration of such services across the country which have led to a significant reduction in the national prevalence **[29]**. Despite these interventions and global recommendations, there is still scarcity of good reliable data from population-based studies to aid implementation of the treatment guidelines, strategy development and resource allocation by the health care providers and policy developers. This is evidenced by the inaccurate diagnosis of HBV patients as this remains a significant challenge thus affecting their treatment management and monitoring. Majority of them are wrongly put on medicine due to unavailability of the recommended diagnostic tests at the health facilities, their high costs and limited access, lack of skills among healthcare workers and furthermore other HBV clients are not given drugs due to the same reasons hence affecting the quality of HBV patient management **[5, 30-32]**. This translates into high HBV related morbidity and mortality.

In Yumbe district, a significantly high burden of HBV, with a prevalence of 6.3%, was reported in 2017 (8) with scarce information on the HBV burden being known on the more than 250,000 South Sudan refugees that are hosted by the district **[33]**. Little information remains known on the diagnosis and treatment management of the approximately 340 HBV patients enrolled at the district's largest and only HBV treatment healthfacility. This is not only for appropriate and timely disease management but to help inform allocation of resources at the facilityand district level as well by both the government and supporting donors for improved uptake of hepatitis B services which leads to improved treatment outcomes.

Materials and Methods

Study area

The study was conducted at Yumbe RRH which is in Yumbe district in the Northwestern (West Nile) region of Uganda serving both Ugandan nationals and South Sudan (SSD) nationals, and refugees of Bidibidi refugee camp. The district has a population of 484, 822 (34)among whom 251,663 are females and 233,159 are males. This is in addition to the over 270,000 refugees, making it the world's second largest camp- Bidibidi, that also refers all its HBV positive screened patients to this hospital for care (35).

Yumbe is bordered by Maracha and Koboko districts in the west, Terego district in the south, Moyo and Obogi districts in the east and South Sudan in the north and all these are under the RRH's catchment area. Yumbe district consists of 3 counties (Aringa south, Aringa North and Aringa Central), 3 health sub districts, 13 sub-counties, 101 parishes, 636 villages and these are served by 46 functional health facilities (HFs) (1 RRH, 2 HC IVs, 26 HC IIIs and 17 HC IIs).

Study design, sample size, sampling procedure and data collection tools

This was a cross sectional study between July- August 2022 to obtain 199 patient records beginning with the oldest patient record. Using the World Health Organization's proportion formula for sample size determination in health studies as stated by Kasiulevicus, Sapoka and Filipaviciute, R (2006) and for calculating the required sample size when the population is < 10,000 by Taofeek (2009), a sample of 180 patient files was obtained considering a CI level of 95% and margin error of 5% which increased to 200 when a 10% missingness of files was incorporated. This method was used because a given sample size provides proportionately more information for a small population. Additionally, Yumbe RRH was purposively selected because it is the only healthcare facility that offers hepatitis B treatment, with all the required facilities and equipment for the recommended treatment eligibility tests in the district. Demographic and patients' data regarding the HBV services consumed was collected from the patient's files/registers at the HBV clinic and the laboratory using a pretested checklist that was developed by the researchers after a relevant literature review. The data collection tool included questions on socio-demographics and a number of recommended treatment eligibility tests consumed by the patients. This was then entered into KoboCollect, a mobile application using a laptop powered with data for real-time upload to the server account to avoid its loss. Besides, the mobile data collection data tool was designed with quality checks to minimize errors and incorrect data entries.

Study variables

The independent variables were patient's socio-demographics such as age, sex, timing of the tests, HBV/HIV coinfection status, patient's duration in care, distance to the hospital and time lag between testing and treatment initiation. The dependent variables included the proportion of tests received (test result on record; Yes -1, No- 0). The proportion of tests received was determined by the number of test results traceable in the HMIS tools out of the total four expected results. Time lag between diagnosis and treatment was determined by using recorded dates of the test results and date HBV treatment was

offered to the patient. The distance to the hospital was estimated in kilometers (km) using google maps with reference to the village of origin of each patient.

Data management and statistical analysis

Data was collected using the KoboCollect mobile application and then exported to STATA 14.0 for statistical analysis. This was password protected and only accessible to the researchers. The online tool was preset with data quality checks to minimize errors.

Ethical statement

Ethical approval was obtained from the Makerere University School of Public Health Higher Degrees and Research Ethics Committee (MakSPH HDREC). Permission to collect data from the hospital was obtained from the Yumbe regional referral hospital administration.

Results

A total number of 318 patient records were reviewed with 119 patient records missing both key variables of interest i.e sex and age and thus were excluded from the study. Only 199 records were eligible for study inclusion, however, 77 records had at least one variable of interest.

6.1 Socio-demographic characteristics of the patients

The mean age of patients was 31.2 (SD 11.2) years. The average distance to the hospital was 9.5 (SD 7.4) kilometers, with 0.1km being the minimum and 40km the maximum distance. Almost half (47.7%) of the patients sampled came from less than 10 kilometers from the hospital. The distance travelled by 25.1% (50/199) of the patients could not be established since their records lacked their respective village names. The average duration in care was 4.1 (SD 1.5) years with the least duration as 0.25 years and the maximum duration in care as 11 years (**table 1** below).

Table 1: Socio-demographic characteristics of patients

Variables	**Category**	**Frequency (n=199)**	**Percentage (%)**
Sex	Female	87	43.7
	Male	112	56.3
Age (years)	0 - 19	24	12.1
	20 - 29	70	35.2
	30 - 39	62	31.2
	40 - 49	29	1.5
	50 - 59	11	5.5
	≥ 60	3	1.5
Average Distance from hospital (km) (measured using google maps)	0 - 10	95	47.7
	11 - 20	43	21.7
	21 - 30	3	1.5
	≥ 30	8	4.0
	Unknown	50	25.1

6.2 Uptake of recommended hepatitis B treatment eligibility tests among HBV patients attending the hepatitis B clinic at Yumbe hospital

CBC was the mostly consumed test with 38.2% (76/199) patients having a result on record while USS was the least consumed with only 7.0% (14/199) patients having results. Only 7.5% (15/199) of the patients had HIV test results with 33.3% (5/15) being HIV/HBV coinfected. In addition, only 26.6% (53/199) of the patients had at least one test result on record. Out of the 199 patients, only 1.01% (2/199) received all the 4 recommended diagnostic hepatitis B tests. Table 2 shows that approximately two thirds, 61.3% (122/199) of the patients did not uptake any main recommended diagnostic test (either CBC or LFTS test) as there were no recorded results on their treatment records, nor could they be traced in the laboratory register. Only about one third, 31.2% (62/199) of the patients had at least one main recommended test (either CBC or LFTS test) taken while only 7.5% (15/199) had both tests. It was also not possible to determine when 124/199 (62.31%) of patients up took the recommended tests since it could not be ascertained if it was before or during treatment initiation. However, 29.7% (59/199) patients took these tests before treatment initiation which is recommended as per the WHO and MOH HBV treatment and management guidelines **(table 2)**.

Table 3 below shows the distribution of hepatitis B treatment eligibility tests by background characteristics

Table 2: Uptake of recommended hepatitis B treatment eligibility tests among HBV patients attending the hepatitis B clinic at Yumbe hospital

Test done and recorded	**Category**	**Frequency (n=199)**	**Percentage (%)**
Complete Blood count (CBC)	Yes	76	38.2
	No	123	61.8
Liver Function tests (LFTs)	Yes	16	8.0
	No	183	92.0
HIV	Yes	15	7.5
	No	184	92.5
Ultra Sound Scan (USS)	Yes	14	7.0
	No	185	93.0
Total number of tests done on patient	0	116	58.3
	1	53	26.6
	2	24	12.1
	3	4	2.0
	4	2	1.0
HIV/HBV coinfection	Yes	5	2.5
	No	10	5.0
	unknown	184	92.5
At least main recommended test done and recorded on file	None	122	61.3
	Only one main recommended test (either LFTs and or CBC)	62	31.2
	Two main recommended tests (both CBC and LFTs)	15	7.5
Eligibility tests done before, during or after treatment initiation	Before	59	29.7
	During	16	8.0
	Unknown	124	62.3

Table 3: Distribution of hepatitis B tests by background characteristics.

Variable	**Main recommended test tests (CBC and LFTS) done**			**Recommended tests done**			
	None	**1**	**2**	**CBC**	**LFTS**	**HIV**	**USS**
Sex	**n**	**n**	**n**	**(n=76) %**	**(n=16)%**	**(n=15)%**	**(n=14)%**
Female	53	25	9	33 (43.4)	10 (62.5)	9 (60.0)	7 (50.0)
Male	69	37	6	43 (56.6)	6 (37.5)	6 (40.0)	7 (50.0)
Age (years)							
0 - 19	15	5	4	9 (11.8)	4 (25.0)	0 (0.0)	1 (7.1)
20 - 29	41	24	4	25 (32.9)	4 (25.0)	8 (53.3)	4 (28.6)
30 - 39	38	22	3	25 (32.9)	4 (25.0)	4 (26.7)	6 (42.9)
40 - 49	22	6	1	11 (14.5)	1 (6.25)	1 (6.7)	1 (7.1)
≥50	6	5	3	6 (7.9)	3 (18.75)	2 (13.3)	2 (14.3)
timing of tests							
Before treatment	9	43	8	50 (65.8)	8 (50)	12 (80.0)	4 (28.6)
During treatment	5	9	2	1 (1.3)	2 (12.5)	2 (13.3)	9 (64.3)
Unknown	108	10	5	15 (19.7)	6 (37.5)	1 (6.7)	1 (7.1)

HIV/ HBV Coinfected							
No	1	9	3	3 (4.0)	0 (0.0)	5 (33.3)	2 (14.3)
Yes	1	5	00	8 (10.5)	3 (18.75)	10 (66.7)	2 (14.3)
Unknown	120	48	12	65 (85.5)	13 (81.25)	0 (0.0)	10 (71.4)
Duration in care							
< 2	1	5	3	6 (7.9)	3 (18.75)	5 (33.3)	2 (14.3)
2 - 4	32	37	7	48 (63.2)	7 (43.75)	8 (53.3)	3 (21.4)
≥ 4	61	8	0	7 (9.2)	0 (0.0)	0 (0.0)	7 (50.0)
Unknown	28	12	5	15 (19.7)	6 (37.5)	2 (13.3)	2 (14.3)
Average Distance from Hospital (km)							
0 – 10	58	35	5	41 (54.0)	7 (43.75)	8 (53.3)	6 (42.9)
11 - 20	25	11	4	13 (17.1)	5 (37.5)	0 (0.0)	2 (14.3)
21 - 30	3	1	0	1 (1.3)	0 (0.0)	0 (0.0)	1 (7.1)
>30	4	1	1	2 (2.6)	1 (6.25)	1 (6.7)	1 (7.1)
unknown	32	14	5	19 (25)	3 (18.75)	6 (40)	4 (28.6)
Time Lag (days)							
0-7	104	30	9	38 (50)	10 (62.50)	10 (66.7)	12 (85.7)
8-14	1	5	0	5 (6.6)	0 (0.0)	0 (0.0)	0 (0.0)
15 -21	6	8	2	8 (10.5)	2 (12.5)	2 (13.3)	1 (7.1)
22 - 28	4	8	1	8 (10.5)	1 (6.25)	1 (6.7)	0 (0.0)
> 28	4	9	3	13 (17.1)	3 (18.75)	3 (20.0)	1 (7.1)
unknown	3	2	0	4 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)

6.3 Bivariable analysis of the factors associated with uptake of HBV treatment eligibility tests

Those associated with the uptake of main recommended treatment eligibility tests were timing of tests ($\chi 2$= 94.9, P< 0.000), co- infection of HIV and HBV ($\chi 2$ = 20.46, P<0.000), duration in care, ($\chi 2$= 68.9, P<0.000), average distance to hospital ($\chi 2$ = 15.5, P<0.017), and time lag ($\chi 2$ = 45.5, P<0.000) **(table 4)**.

Table 4: Factors associated with uptake of major eligibility tests by HBV patients

Variables	**Main recommended eligibility tests done & recorded on file**						**Chi Squar ($\chi 2$)**	**P-Value**
	None n = 122		**One n = 62**		**Two n = 15**			
	n	**%**	**n**	**%**	**n**	**%**		
Sex							1.9104	0.385
Female	53	43.4	25	40.3	9	60.0		
Male	69	56.6	37	59.7	6	40.0		
Age (years)							12.6818	0.242
0 - 19	15	12.3	5	8.1	4	26.7		
20 - 29	41	33.6	24	38.7	4	26.6		
30 - 39	38	31.1	22	35.4	3	20.0		
40 - 49	22	18.0	6	9.7	1	6.7		
≥50	6	5.0	5	8.1	3	20		
timing of tests							**94.9484**	**0.000 *****
Before treatment	9	7.4	43	69.4	8	53.3		
During treatment	5	4.1	9	14.5	2	13.3		
Unknown	108	88.5	10	16.1	5	33.3		

HIV/ HBV Coinfected							**20.4611**	**0.000*** **
No	1	0.8	9	14.5	3	20.0		
Yes	1	0.8	5	8.1	0	0.0		
Unknown	120	98.4	48	77.4	12	80.0		
Duration in care							**68.9423**	**0.000*** **
< 2	1	0.8	5	8.0	3	20.0		
2 - 4	32	26.2	37	59.7	7	46.7		
≥ 4	61	50.0	8	13.0	0	0.0		
Unknown	28	23.0	12	19.3	5	33.3		
Average Distance from Hospital (km)							**15.5116**	**0.017*** **
0 – 10	58	47.5	35	56.5	5	33.3		
11 - 20	25	20.5	11	17.7	4	26.7		
21 - 30	3	2.5	1	1.6	0	0		
>30	4	3.3	1	1.6	1	6.7		
unknown	32	26.2	14	22.6	5	33.3		
Time Lag (days)							**45.4674**	**0.000*** **
0-7	104	85.2	30	48.4	9	60.0		
8-14	1	0.8	5	8.1	0	0.0		
15 -21	6	5.0	8	13.0	2	13.3		
22 - 28	4	3.0	8	13.0	1	6.7		
> 28	4	3.0	9	14.5	3	20.0		
unknown	3	3.0	2	3.0	0	0		
*** Level of Significance = 0.05								

6.4 Multivariable analysis of factors associated with uptake of recommended treatment eligibility tests

At the multivariable analysis level (**table 5** below), the factors that were associated with the uptake of main recommended tests were (see **table 5** below): timing of tests (IRR = 0.44, 95% CI 0.21 – 0.92). There is a relationship in the population between the time when monitoring is done and the uptake of main recommended eligibility tests for HBV treatment.

Patients that took tests before treatment initiation were 5.8 times more likely to have a main recommended eligibility test done than those whose timing of the tests was unknown (IRR= 5.8, 95% CI 3.52 - 9.56). In addition, patients that took tests after treatment initiation were 4.8 times more likely to have a main test done than those whose timing of tests was unknown (IRR =4.79, 95% CI 2.40- 9.58) **(table 6)**.

Table 5: Predictors of HBV diagnostic tests uptake.

Main recommended test done	IRR	Std. Err.	z	P>z	[95% Conf. interval)
CBC/LFT done prior to initiation or during treatment	**0.44**	**.1667041**	**-2.17**	**0.030**	**(0.21- 0.92)**
HIV/HBV Coinfection	1.10	.0571778	1.51	0.131	(0.98 - 1.20)
Duration in Care	0.91	.2576925	-0.37	0.709	(0.51- 1.58)
Average Distance to hospital	0.90	.1528718	-0.61	0.539	(0.65 - 1.26)
Time Lag	1.03	.0952676	0.32	0.746	(0.86 - 1.24)
_cons	0.55	.4480196	-0.73	0.463	(0.11 – 2.72)

Table 6*:* Showing variation within patients that were offered tests at different times

Recommended diagnostic test done and recorded	IRR	Std. Err.	z	P>z	[95% Conf. Interval]
Tests done at unknown time					
Before treatment initiation	**5.80**	**1.478319**	**6.91**	**0.000**	**(3.52 - 9.56)**
After treatment initiation	**4.79**	**1.693105**	**4.44**	**0.000**	**(2.40 - 9.58)**
_cons	0.169	.0369563	-8.14	0.000	(0.11- 0.26)

Discussion

More than half of the patients (58.3%) did not have a recommended HBV treatment eligibility test result. During data collection, a lot of data was missing as good record keeping practices were not evident. This could be attributed to the use of non-authorized Health Management Information System (HMIS) tools such as improvised counter books which lacked many vital parameters such as tests consumed, villages of origin of the patients among others. The completed registers could not easily be retrieved due to absence of an archival section/room at all the departments. Also, none of the departments had an independent records officer or data clerk dedicated to data and information management despite this being a regional referral hospital.

Interestingly, there were more records for men (56.3%) than women (43.7%). These findings agree with those from previous HBV related studies **[36,37]**. This could be explained by both system and gender related factors such as males' economic ability to afford the tests outside the facility when the facility has stock out of laboratory reagents as well as maneuver the healthcare system flow. In addition, males are less affected by the cultural practices since they do not have to seek permission from anyone to seek medical care **[38]**.

CBC was the mostly consumed test (38.2%). This could be attributed to the regular availability of test reagents, staff competency in interpreting its results, its availability and affordability in the private clinics outside the hospital as well the short duration of test analysis as reported in other related previous studies **[39,40]** These findings, however, are not in agreement with those that reported limited lack of knowledge among HCWs as the factor for poor HBV service uptake **[41,42]**

Despite the availability of three functional USS machines, USS was the least provided (7.0%), and this could be due to the acute staff shortage in the department and chronic power shortage in the hospital as elaborated among the barriers to the provision of HBV diagnostic services by both the KIs and the HCWs in the FGD. Such findings related with previous studies **[43]**. Only 1% (2/199) of the patients had taken all the four **[4]** recommended HBV tests. This could have been more, however, the poor record keeping and lack of individual patient files may be attributed to this as there were many results in the laboratory registers that did not have linkage with the patient records such as the dispensing logs and appointment registers in the ART clinic.

Only 31.2% (62/199) of the patients had received either CBC and or LFTS tests (main recommended test) while 7.5% (15/199) had both tests. Despite these two tests being key determinants of HBV treatment eligibility since they are needed to determine APRI Score, their uptake was still very low. The FGD participants highlighted the regular stock out of commodities and equipment breakdown that significantly affected equipment utilization and thus low service uptake. Such similar challenges have been reported in other studies **[44]**.

Well as HCWs demonstrated knowledge on diagnosis and management of HBV infection, low HIV screening was reported among HBV patients at 7.5%. The gross shortage of human resource at the hospital especially the ART clinic may be blamed for this as the few available HCWs could be overwhelmed by the over flow of both HIV and HBV that are assessed at every clinic day making them concentrate on only dispensing of drugs for the HBV patients and leaving out the screening for the HIV/HBV coinfection. Additionally, the non-screening of patients referred from lower health facilities may significantly contribute to this low HIV screening rate.

7.1.2 Predictors of uptake of HBV diagnostic services

At bivariable analysis, sex and age were not associated with uptake of the major HBV treatment eligibility tests. These findings differ from previous related HBV studies **[45,46]**. The uptake of main recommended diagnostic tests (CBC and LFTs) was predicted by; timing of tests ($\chi2$ = 94.9, P< 0.000), HIV/HBV coinfection ($\chi2$ = 20.46, P<0.000), number of tests done ($\chi2$ =265.6, P<0.000), duration in care ($\chi2$= 68.9, P<0.000), average distance to hospital ($\chi2$= 15.5, P<0.017), and time lag between diagnosis and treatment initiation ($\chi2$= 45.5, P<0.000). Although these factors were significant at bivariable, they were not statistically significant at multivariable analysis with the exception of timing of the main recommended diagnostic tests (IRR = 0.44, 95% CI 0.21 – 0.92).

Interestingly, well as we could not tell when majority (62.3%) of the tests were done (unknown= 124/ 199), the timing of these tests was associated with their uptake. The number of tests done before treatment initiation (29.7%) were more than three times those done after/during treatment monitoring (8.0%). This was an indication of the right implementation of the WHO and MOH guidelines that require determination of the liver disease progress to initiate or differ

HBV treatment **[12,14]**. This may be explained by the more time allocated by HCWs to patients' counselling immediately after testing HBV positive and diagnosis as compared to that during routinedisease monitoring. Patients may be more willing to wait and undergovarious other tests just immediately after testing positive than on other consecutive appointment dates during the treatment monitoring phase. This could also be attributed to the community sensitization that was reported as key facilitator for the demand and consequently provision of these services at Yumbe RRH which enables patients acquire willingness to interact with the service providers on diagnosis date to acquire more information than later in the continuum of care. These findings may be related with those reported by (47)where prompt action by physicians increased HBV vaccination uptake.

This study also documents HIV/HBV coinfection as a predictor of service uptake ($\chi 2$= 20.46, P<0.000). However, this was not statistically significant at multivariable analysis. This is probably because co-infected patients are more likely to visit the facility frequently and thus receive diagnostic services than mono infected patients. The coinfection rates were higher (2.5%) than those reported in a related study (0.6%) conducted among a general population in a rural setting in Uganda **[48]**. This high coinfection rate may be because this study was conducted among already diagnosed patients and not a general population. Additionally, this could be because the clinicians are able to comprehensively screen and diagnose the known co-infected patients so that they are initiated on the correct and right treatment.

After further multivariable analysis, patients who were offered HBV tests before treatment initiation were approximately six times more likely to have a main recommended HBV test (either CBC and/or LFTs) than those whose timing of tests was unknown (IRR =5.80, 95% CI 3.52 – 9.56) **(table 6)**. This is correct in reference to the WHO and MoH guidelines so that the extent of liver damage is determined and for guidance of clinical decision making **[12,14]**. Such patients may have better treatment outcomes compared to their counterparts since the stage of liver disease is determined prior to treatment initiation.

Strengths and limitations of the study.

This was the first study of a kind at this rural hospital and thus these findings could be useful in establishing preliminary evidence for planning of future advanced studies. Additionally, the number of records reviewed (sample size used) was close to the patient population size, however, these results may not be inferred to other populations. The principal limitation was poor record keeping that hindered collection of all the data variables required. Many of the patients' records had missing data as they did not have specific files for their management and instead dispensing, and laboratory registers were used to trace most records. The evident use of improvised data tools such as counter books was frequent and these lacked majority of the variables of interest, further constraining efforts to retrieve and collect required data with ease. Therefore, the lack of vital data on many patients led to uncertainty regarding the quality of care they are being provided. This was perhaps because there are no such dedicated HIMS tools that have been developed for the hepatitis B program by the Ministry of Health.

Conclusion and recommendations

There was sub optimal uptake of HBV treatment eligibility tests by HBV patients at YRRH, with CBC being the mostly consumed while USS was least consumed test. There is also evidence of underscreening for HIV/HBV coinfection among patients despite HCWs knowledge of the WHO recommended diagnosis and treatment guidelines. Thus, HCWs should endeavor to provide all the eligibility tests before HBV treatment initiation for appropriate clinical management of the patients. There was evidence that different health IPs extend support to the hospital in various kinds, however, this is not sustainable and thus need for MoH and hospital ownership of hepatitis B programming.

However, strengthened community sensitization should be strengthened as it greatly contributes to demand of HBV services and thus their uptake.

The hospital management and MoH should identify strategies of always ensuring availability of HBV related commodities such as pediatric treatment regimens and laboratory reagents to improve service uptake.

The staffing levels of the hospital should be addressed to improve efficiency in the diagnosis and management of HBV patients. This should cater for inclusion of data clerks and records officers tomanage patient information and record keeping as per the MOH guidelines.

Declaration

Ethical Approval and consent to participate

Ethical approval was obtained from Makerere University School of Public Health Higher Degrees and Research Ethics Committee (MakSPH HDREC). Permission to collect data from the hospital was obtained from the Yumbe regional referral hospital administration. Informed consent was obtained from FGD participants and KIs after the researcher explained the purpose of the study.

Consent to Publication: Not applicable.

Data Availability Statement (DAS)

The datasets generated and/or analysed during the current study are available in the figshare repository under Digital Object Identifier (DOI) link 10.6084/m9.figshare.24155520

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Author Contribution

FM conceptualized the study, developed the data collection tools, analyzed the data and wrote the draft manuscript. FM, AJ, AF, RN pretested the tools and collected the data. JNM, MN, TS, NR peer reviewed the draft manuscript. All authors have read and approved the manuscript

Abbreviations

HBV - hepatitis B Virus

YRRH- Yumbe Regional Referral Hospital

FGD - Focus Group Discussion

KI- Key Informant

CBC - Complete Blood Count

PR -Prevalence Ratio

HCWs -Health Care Workers

References

1. World Health Organisation W. Hepatitis B; Key facts. 2021.
2. World Health Organization (2017) Global hepatitis report 2017: World Health Organization.
3. Spearman CW, Afihene M, Ally R, Apica B, Awuku Y, et al. (2017) Hepatitis B in sub-Saharan Africa: strategies to achieve the 2030 elimination targets. The Lancet Gastroenterology & Hepatology. 2(12): 900-909.
4. GBD 2016 Causes of Death Collaborators (2017) Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet. 390(10100): 1151-210.
5. O'Hara GA, McNaughton AL, Maponga T, Jooste P, Ocama P, et al. (2017) Hepatitis B virus infection as a neglected tropical disease. PLoS neglected tropical diseases. 11(10): e0005842.
6. Bwogi J, Braka F, Makumbi I, Mishra V, Bakamutumaho B, et al. (2009) Hepatitis B infection is highly endemic in Uganda: findings from a national serosurvey. African health sciences. 9(2): 98-108.
7. Ministry of Health U. Uganda Population - Based Hiv Impact Assessment. 2019: 1-252.
8. Acheng JR. STATEMENT TO PARLIAMENT OF UGANDA FROM THE HON. PROGRESS ON HEPATITIS B VACCINATION ACTIVITIES IN MINISTER OF HEALTH, DR. JAITE RUTH ACENG ON THE NORTHERN UGANDA. 2017.
9. World Health Organisation W (2017) Guidelines on Hepatitis B and C Testing. 66(February).
10. Cohn J, Owiredu MN, Taylor MM, Easterbrook P, Lesi O, et al. (2021) Eliminating mother-to-child transmission of human immunodeficiency virus, syphilis and hepatitis B in sub-Saharan Africa. Bulletin of the World Health Organization. 99(4): 287.
11. Firnhaber C, Reyneke A, Schulze D, Malope B, Maskew M, et al. (2008) The prevalence of hepatitis B co-infection in a South African urban government HIV clinic. South African Medical Journal. 98(7): 541-544.
12. Ministry of Health MU. The Republic of Uganda. Ministry of Health (2019) Uganda Guidelines for Prevention , Testing , Care and Treatment of Hepatitis B and C Virus Infection.
13. Sun H-Y, Sheng W-H, Tsai M-S, Lee K-Y, Chang S-Y, et al. (2014) Hepatitis B virus coinfection in human immunodeficiency virus-infected patients: a review. World journal of gastroenterology: WJG. 20(40): 14598.
14. World Health Organization W (2015) Guidelines for the prevention care and treatment of persons with chronic hepatitis B infection. World Health Organization.
15. Sonderup MW, Afihene M, Ally R, Apica B, Awuku Y, et al. (2017) Hepatitis C in sub-Saharan Africa: the current status and recommendations for achieving elimination by 2030. The Lancet Gastroenterology & Hepatology. 2(12): 910-919.
16. Brunetto MR, Oliveri F, Colombatto P, Moriconi F, Ciccorossi P, et al. (2010) Hepatitis B surface antigen serum levels help to distinguish active from inactive hepatitis B virus genotype D carriers. Gastroenterology. 139(2): 483-90.
17. Lok AS, McMahon BJ (2009) Chronic hepatitis B: update 2009. Hepatology. 50(3): 661-2.
18. Chen C-J, Iloeje UH, Yang H-I (2007) Long-term outcomes in hepatitis B: the REVEAL-HBV study. Clinics in liver disease. 11(4): 797-816.
19. McNaughton AL, Lourenço J, Bester PA, Mokaya J, Lumley SF, et al. (2020) Hepatitis B virus seroepidemiology data for Africa: Modelling intervention strategies based on a systematic review and meta-analysis. PLoS medicine. 17(4): e1003068.
20. Nankya-Mutyoba J, Aizire J, Makumbi F, Atuyambe L, Kirk G, et al. (2019) Hepatitis B Prevalence among Pregnant Women in Central and West Nile regions of Uganda: Is there a Need to prioritize Prevention of Mother to Child hepatitis B transmission?.
21. Ssekamatte T, Mukama T, Kibira SP, Ndejjo R, Bukenya JN, et al. (2020) Hepatitis B screening and vaccination status of healthcare providers in Wakiso district, Uganda. Plos one. 15(7): e0235470.

22. Ssekamatte T, Isunju JB, Mutyoba JN, Tetui M, Mugambe RK, et al. (2020) Factors associated with Hepatitis B screening and completion of vaccination schedule among young psychoactive substance users in Kampala's informal settlements, Uganda.
23. Ssekamatte T, Isunju JB, Zirimala PAK, Etajak S, Kamukama S, et al. (2021) A positive attitude among primary healthcare providers predicts better hepatitis B prevention practices:evidence from a cross-sectional survey in Wakiso district, CentralUganda. Health Psychol Behav Med. 9(1): 298-314.
24. Omotowo IB, Meka IA, Ijoma UN, Okoli VE, Obienu O, et al. (2018) Uptake of hepatitis B vaccination and its determinants among health care workers in a tertiary health facility in Enugu, South-East, Nigeria. BMC Infect Dis. 18(1): 288.
25. Jepkios Bett L (2015) Uptake Of Hepatitis B Vaccination And Its Determinants Among High Risk Health Care Workers In Selected Hospitals In Kenya. A Research Thesis Submitted in Partial Fulfillment of the Requirements for the Award of the Degree of Master of Public Health and Epidemiology in the School of Public Health of Kenyatta University.
26. World Health Organization (2016) Global health sector strategy on viral hepatitis 2016-2021. Towards ending viral hepatitis. World Health Organization.
27. Cooke GS, Andrieux-Meyer I, Applegate TL, Atun R, Burry JR, et al. (2019) Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission. The Lancet Gastroenterology & Hepatology. 4(2): 135-84,.
28. Ministry of Health (2002) UGANDA NATIONAL EXPANDED PROGRAM ON IMMUNISATION (UNEPI).
29. Ministry of Health (2018) World Hepatitis Day 2018: Press statement on the progress of implementation of Hepatitis B vaccination program in Uganda. 2018: 1-7.
30. Trinh-Shevrin C, Pollack HJ, Tsang T, Park J, Ramos MR, et al. (2011) The Asian American hepatitis B program: building a coalition to address hepatitis B health disparities. Prog Community Health Partnersh. 5(3): 261-71.
31. Laing N, Tufton H, Ochola E, P'Kingston OG, Maini MK, et al. (2019) Hepatitis B assessment without hepatitis B virus DNA quantification: a prospective cohort study in Uganda. Trans R Soc Trop Med Hyg. 113(1): 11-17.
32. Waheed Y, Siddiq M, Jamil Z, Najmi MH (2018) Hepatitis elimination by 2030: Progress and challenges. World J Gastroenterol. 24(44): 4959-61.
33. Isadru VR, Nanyonga RC, Alege JB (2021) Health Facilities' Readiness to Manage Hypertension and Diabetes Cases at Primary Health Facilities in Bidibidi Refugee Settlement, Yumbe District, Uganda. Journal of Tropical Medicine. 2021(1): 1-10.
34. UBOS (2017) National population and housing census 2014: Area specific profiles. Author Kampala, Uganda.
35. United Nations High Commissioner for Refugees (2019) Uganda Country Refugee Response Plan: The Integrated Response Plan for Refugees from South Sudan, Burundi and the Democratic Republic of the Congo. January 2019–December 2020.
36. Gilbert RL, Costella A, Piper M, Gill ON (2004) Increasing hepatitis B vaccine coverage in prisons in England and Wales. Commun Dis Public Health. 7(4): 306-11.
37. Hutchinson SJ, Wadd S, Taylor A, Bird SM, Mitchell A, Morrison DS, et al. (2004) Sudden rise in uptake of hepatitis B vaccination among injecting drug users associated with a universal vaccine programme in prisons. Vaccine. 23(2): 210-4.
38. Konopnicki D, Mocroft A, de Wit S, Antunes F, Ledergerber B, et al. (2005) Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort. Aids. 19(6): 593-601.
39. Bini EJ, Kritz S, Brown LS Jr, Robinson J, Calsyn D, et al. (2012) Hepatitis B virus and hepatitis C virus services offered by substance abuse treatment programs in the United States. J Subst Abuse Treat. 42(4): 438-45.
40. Alege JB, Gulom G, Ochom A, Kaku VE (2020) Assessing Level of Knowledge and Uptake of Hepatitis B Vaccination among Health Care Workers at Juba Teaching Hospital, Juba City, South Sudan. Adv Prev Med. 2020: 8888409.
41. Lee ACK, Vedio A, Liu EZH, Horsley J, Jesurasa A, et al. (2017) Determinants of uptake of hepatitis B testing and healthcareaccess by migrant Chinese in the England: a qualitative study. BMC Public Health. 17(1): 747.
42. Boye S, Shimakawa Y, Vray M, Giles-Vernick T (2020) Limited Awareness of Hepatitis B but Widespread Recognition of Its Sequelae in Rural Senegal: A Qualitative Study. Am J Trop Med Hyg. 102(3): 637-43.
43. Subic M, Zoulim F (2018) How to improve access to therapy in hepatitis B patients. Liver Int. 38(Suppl 1): 115-21.
44. Freeland C, Bodor S, Perera U, Cohen C (2020) Barriers to Hepatitis B Screening and Prevention for African Immigrant Populations in the United States: A Qualitative Study. Viruses. 12(3): 305.
45. Seetharam A, Perrillo R, Gish R (2014) Immunosuppression in patients with chronic hepatitis B. Current hepatology reports. 13(3): 235-44.
46. Yang JD, Gyedu A, Afihene MY, Duduyemi BM, Micah E, et al. (2015) Hepatocellular Carcinoma Occurs at an Earlier Age in Africans, Particularly in Association With Chronic Hepatitis B. Am J Gastroenterol. 110(11): 1629-31.
47. Vedio A, Liu EZH, Lee ACK, Salway S (2017) Improving access to health care for chronic hepatitis B among migrant Chinese populations: A systematic mixed methods review of barriers and enablers. J Viral Hepat. 24(7): 526-40.

48. Apecu R, Bagenda F, Byarugaba F, Bum I (2018) Human Immunodeficiency Virus and Hepatitis B Virus Co-infection: A Cross-sectional Household Survey in Kiruhura District, Southwestern, Uganda. International Journal of Tropical Disease & Health. 30(2): 1-12.