

## Review

# The risk of mother-to-child transmission of hepatitis B virus infection in Ethiopia: A systematic review and meta-analysis

Belaynew W Taye<sup>1,2</sup>, Girum M Ayenew<sup>3</sup>, Zewdu Wasie Taye<sup>4</sup>, Melashu Balew<sup>3</sup>, Eden Bishaw Taye<sup>5</sup>

<sup>1</sup> Telethon Kids Institute, Wesfarmers Centre of Vaccines and Infectious Diseases, Infectious Disease Epidemiology Team, Perth, Australia

<sup>2</sup> Curtin School of Population Health, Curtin University, Perth, Australia

<sup>3</sup> Amhara Public Health Institute, Bahir Dar, Amhara, Ethiopia

<sup>4</sup> Health Department, International Red Cross Society, North Gondar, Amhara, Ethiopia

<sup>5</sup> College of Medicine and Health Sciences, The University of Gondar, Gondar, Ethiopia

### Abstract

**Introduction:** Mother-to-child transmission (MTCT) of hepatitis B virus (HBV) is a predominant route of infection for children in Ethiopia. No study has so far reported a nationwide estimate of the risk of MTCT of HBV. We conducted a meta-analysis of surveys and estimated the pooled risk of MTCT of HBV in the context of human immunodeficiency virus (HIV) infection.

**Methodology:** We searched PubMed, EMBASE, Web of Science, Africa Index Medicus, and Google Scholar databases for peer-reviewed articles. The pooled risk of MTCT of HBV was estimated using the DerSimonian-Laird technique with logit transformed proportions and statistical heterogeneity was estimated using  $I^2$  statistic, which was explored by subgroup and meta-regression analyses.

**Results:** The overall pooled risk of MTCT of HBV in Ethiopia was 25.5% (95% CI, 13.4%–42.9%). In women without HIV infection, the risk of MTCT of HBV was 20.7% (95% CI 2.8%–70.4%), and 32.2% (95% CI 28.1%–36.7%) in women with HIV infection. After excluding the outlier study, the risk of MTCT of HBV in studies that included only HIV negative women was 9.4% (95% CI, 5.1%–16.6%).

**Conclusions:** The risk of MTCT of HBV in Ethiopia widely varied by HBV/HIV coinfection. A sustainable control and elimination of HBV in Ethiopia requires improved access to birth-dose HBV vaccine and implement immunoglobulin prophylaxis for exposed infants. Given the limited health resources in Ethiopia, prenatal antiviral prophylaxis integrated with antenatal care may be a cost-effective approach to significantly reduce the risk of MTCT of HBV.

**Key words:** elimination; mother-to-child transmission; hepatitis B, meta-analysis; meta-regression.

*J Infect Dev Ctries* 2023; 17(6):744-751. doi:10.3855/jidc.17931

(Received 13 January 2023 – Accepted 07 March 2023)

Copyright © 2023 Taye *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Introduction

Hepatitis B virus (HBV) infection is one of the leading underlying risk factors for the development of hepatocellular carcinoma [1]. Globally in 2019, 296 million people were living with HBV infection. Chronic HBV has caused more than 820,000 deaths mostly from hepatocellular carcinoma and decompensated cirrhosis of the liver [2]. Ethiopia has a high population prevalence of HBV infection, with an estimated 6% of the population positive for HBsAg [3]. In pregnant women in Ethiopia, the burden of HBV infection is higher than that in the general population at an estimated prevalence of 7.9% [4].

Mother-to-child transmission (MTCT) of HBV contributes significantly to HBV infection worldwide and accounts for more than 50% of the global HBV burden [5]. Mother-to-child transmission is the most

prevalent route of infection through which children acquire HBV in Ethiopia. Ethiopia implemented infant HBV vaccination in 2007, which was aimed at reducing the burden of HBV infection and HBV-related liver disease in the population [6]. Children who acquire HBV through MTCT often develop chronic HBV in more than 90% of infections. HBV infection in early childhood that results in a long duration of chronic HBV is associated with younger age at onset of hepatocellular carcinoma and early mortality compared to other regions [7-9].

Despite the implementation of infant vaccination in the national expanded program of immunization, the prevalence of HBV remains high [10], partly because of the persistently high rates of MTCT, which continues to significantly contribute to the endemicity of HBV in Ethiopia. The high rate of HBV/HIV co-infection in

Ethiopia contributes to the persistently high rate of vertical transmission of HBV to exposed infants [11]. There are few studies to date that determined the rate of MTCT of HBV in Ethiopia. Of note, the studies employed small samples of pregnant women diagnosed with HBV, and the rates may not reflect the national estimate of the risk of vertical transmission due to very diverse healthcare access and sociocultural determinants of health across regions. Moreover, the studies that determined MTCT risk were conducted in specific community settings or at healthcare facilities and may not be representative of the wider geography of the country. A pooled estimate of the risk of MTCT from several studies in a meta-analysis addresses the questions of sample size and inter-regional variation and may provide a more representative estimate of the transmission risk to inform decision-making. In a meta-analysis study of observational studies in Ethiopia, we estimated the risk of MTCT of HBV in children born to women with HBV.

## Methodology

### *Literature search strategy*

We followed the preferred reporting items for systematic review and meta-analysis (PRISMA) 2009 statement and the PRISMA 2020 updated guidelines to conduct this meta-analysis [12,13]. The protocol was registered in the prospective register of systematic reviews (registration number: CRD42021284704).

We searched PubMed, EMBASE, Web of Science, Africa Index Medicus, and Google Scholar databases for published observational studies on MTCT of HBV in Ethiopia. We used both free-text and Medical Subject Heading (MeSH) terms for ‘hepatitis B virus’ OR ‘hepatitis B’, ‘vertical transmission’ OR ‘mother-to-child transmission’, and ‘Ethiopia’. Detailed search terms for all databases are available in Supplementary Table 1.

### *Selection criteria*

We included studies that assessed HBV vertical transmission and published in English between January 1, 1980, and September 30, 2021. We considered primary observational studies that employed cross-sectional, comparative cross-sectional, survey, retrospective or prospective cohort designs and conducted in a clinical or community-based setting. Pregnant women with HBV infection were included irrespective of their HIV status, and whether they had a history of receipt of antiviral prophylaxis during pregnancy. We excluded narrative reviews, case

reports, editorials and letters to the editor, commentaries, viewpoints, and systematic reviews.

All records retrieved from the search databases were exported to EndNote 20. First, duplicate records were removed from the combined database and screened for their relevance to the aim of the study using title and abstract - records not relevant to the MTCT of HBV were excluded. We examined the full text of the remaining studies in detail to assess their eligibility. Finally, we assessed the methodological quality of studies that fulfilled the inclusion criteria and included them in the meta-analysis.

### *Study outcomes*

The primary outcome of the study was MTCT of HBV. Mother-to-child transmission of HBV was defined as a positive HBsAg test in a child born to a mother with HBsAg. HBsAg tests for HBV-exposed infants were measured from birth to 24 months of age. Study level variables that might be the source of heterogeneity were maternal HBeAg positivity, HIV status, presence of antiviral prophylaxis during pregnancy, birth dose vaccine for the newborn, and year of study.

### *Data extraction and quality assessment*

The methodological quality and risk of bias of included studies were assessed using the New Castle-Ottawa Scale (NOS) for quality assessment of observational studies [14]. We applied the modified NOS to assess the methodological quality of cross-sectional studies [15]. Using the guidelines for scoring utilizing this scale, we rated the quality of included articles and presented them in a table.

We extracted data for study-level variables relevant to the meta-analysis using a standard electronic data extraction form created in Microsoft Excel. We included study identification, year of study, percentage of HIV-positive samples, percentage HBeAg positive, percentage of HBV-positive women who received antiviral prophylaxis, sample size, number of children HBV positive, and NOS quality score. We also included information on infant vaccination and birth dose vaccination.

### *Data synthesis and meta-analysis*

We used the *metaprop* program of R software version 4.1.1 (The R Foundation for Statistical Computing 2021) to perform the meta-analysis. A random-effects meta-analysis was used to estimate the risk of MTCT of HBV because of the expected variation between studies. A subgroup analysis was performed to

explore heterogeneity and obtain the risk of transmission in studies that included HIV positive women and studies that included only HIV negative women.

Logit transformation was used to transform the proportion of vertical transmission of HBV. Pooled estimates of the risk of MTCT of HBV were performed using DerSimonian–Laird non-iterative weighted estimates technique. 95% confidence intervals (CI) were calculated using the exact method. A *p* value < 0.05 was used to determine a statistically significant association. We used forest plots to depict the risk of MTCT of HBV in all studies and by subgroups. The heterogeneity between included studies was measured by *I*<sup>2</sup> statistics, and subgroup analysis was used to evaluate the heterogeneity. We performed meta-regression to identify study-level factors contributing to heterogeneity [16].

**Results**

*Study selection*

Figure 1 illustrates the detailed study identification and selection process using the PRISMA guidelines. We retrieved a total of 83 records from all search engines published between January 1, 1980, and September 30, 2021. A total of 39 duplicate records were initially excluded. The full text of forty-four studies was assessed for eligibility, and a total of 38 studies did not fulfill inclusion criteria (4 studies were on Ethiopians living abroad, one study on blood donors, five studies assessed HBV/HIV coinfection, six studies were on HCV/HBV coinfection, and 22 studies were prevalence surveys in different population groups) were excluded. After further eligibility assessment, five studies were included in the systematic review and metaanalysis [17-21]. The quality of included studies ranged from an NOS score of 8 to a score of 11 (Supplementary Table 2).

*Characteristics of included studies*

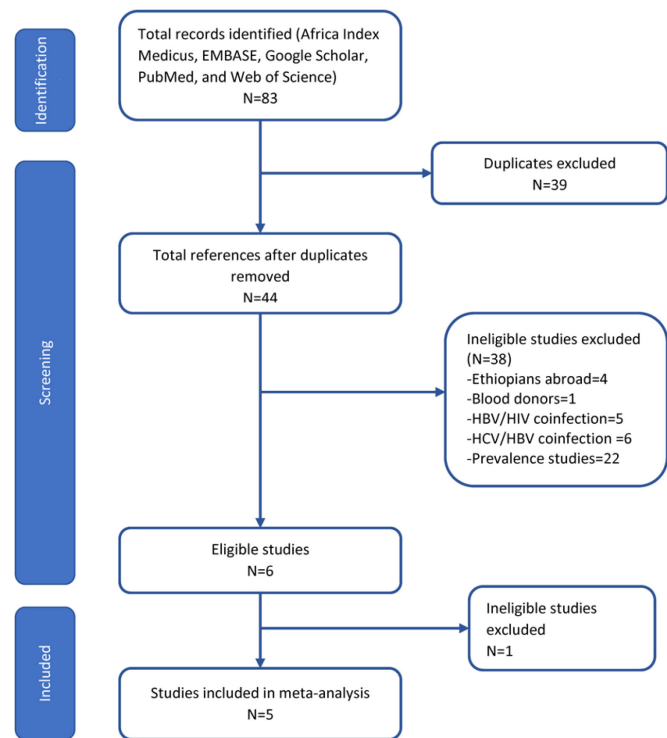
Table 1 presents the characteristics of studies included in the meta-analysis. A total of five observational studies were included in the meta-

analysis. All the studies were conducted in a clinical setting. Three out of five studies [18,20,21] were conducted in the capital city, Addis Ababa, while two were from regional Ethiopia. One study [21] was conducted during the pre-vaccine period. The mean/median age of participating women in included studies was ranged between 23.7 years [21] and 29 years [18]. The presence of HBsAg in newborns was tested from birth to 24 months of age.

*Risk factors and prevention methods for mother-to-child transmission*

The presence of HBeAg was reported in three of the five studies. The highest HBeAg positivity rate (12.5%) was reported by Tegegne *et al.* [20] a study by Johannessen *et al.* reported an HBeAg positivity rate of

**Figure 1.** Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart for study selection and inclusion of studies that reported risk of mother to child transmission of hepatitis B virus in Ethiopia.



**Table 1.** Characteristics of studies included in the meta-analysis of the risk of mother-to-child transmission of hepatitis B virus in Ethiopia.

Study ID	Study period	Region	Study design	Number of HBV+ mothers	Number of children HBsAg+	Assessment methods	Age of mothers (mean/median)	%HBeAg+	% HIV positive	%ARV during pregnancy	% Infant HBV vaccine	Age at assessment of HBV infection
Johannessen 2021	2015	Addis Ababa	Cross-sectional	89	9	HBsAg	29	8.2	0	3.4	15.4	20 months
Kiros 2020	2020	Tigray	Cross-sectional	55	17	HBsAg	26.5	– <sup>a</sup>	10.9	–	–	Birth
Tegegne 2014	2012	Addis Ababa	Cross-sectional	8	6	HBsAg	25.8	12.5	0	–	–	12 months
Tsega 1988	1988	Addis Ababa	Cross-sectional	20	1	HBsAg	23.7	0	0	0	0	24 months
Bayu 2020	2019	Oromia	Cross-sectional	401	130	HBsAg	28.6	–	13.7	–	37.9	Birth to 12 months

<sup>a</sup>Not assessed/not reported.

8.2% [18] and none of the participating women had evidence of HBeAg in a study by Tsega *et al* [21]. A high prevalence of HIV infection was reported in two studies. An estimated 14% of pregnant women were positive for HIV infection in a study by Bayu *et al* [17] followed by about 11% prevalence from a study in Tigray region [19]. A study by Johannessen *et al.* excluded mothers with HIV infection, while in two other studies [20,21] all participant mothers did not have any evidence of HIV infection. Antiviral prophylaxis during pregnancy was provided for 3.4% of pregnant women in one study [18] and no prophylaxis was provided for the other four studies (Table 1) [17,19-21].

*Risk of mother-to-child transmission of hepatitis B*

There were 573 deliveries from pregnant women with HBV infection. A total of 167 newborns were HBV infected. The pooled risk of MTCT of HBV in Ethiopia was estimated at 25.5% (95% CI 13.45 – 42.9%). The lowest risk of MTCT of 5.0% was reported in a study by Tsega *et al* [21]. The highest MTCT rate(32.4%) was reported in a study comprising 401 infants exposed to HBV [17]. An MTCT transmission rate of 75% was reported in a study by Tegegne *et al.* [20], which appears to be an outlier compared with rates from all other studies. We observed a pattern in the rate of MTCT of HBV over time, with lower rates from studies conducted between 1988 and 2015 including those conducted during the pre-HIV epidemic era, while higher rates of MTCT of HBV were reported from studies conducted in recent years [17,19]. The detailed pooled estimate of the rate of MTCT of HBV is presented in Figure 2.

*Subgroup analysis*

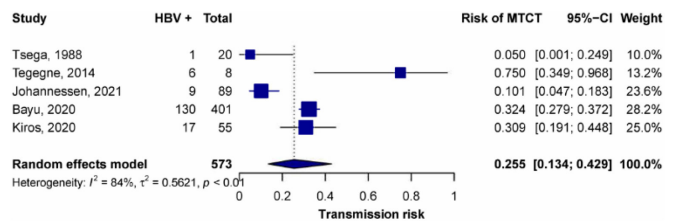
Three studies included women with no HIV infection. One study was conducted before the beginning of the HIV epidemic in Ethiopia [21] and another study recruited women with a negative HIV test [18], while the third study [20] reported an HIV prevalence of zero. In the HIV negative group, the pooled estimate of the risk of MTCT of HBV was 20.7%.

Two studies included women with HIV infection, reporting a prevalence of 10.9% [19] and 13.7% [17]. For studies that included women with HIV infection, the risk of MTCT for HBV was one-in-three deliveries (estimate = 32.2%, 95% CI 28.1 –36.7) (Figure 3).

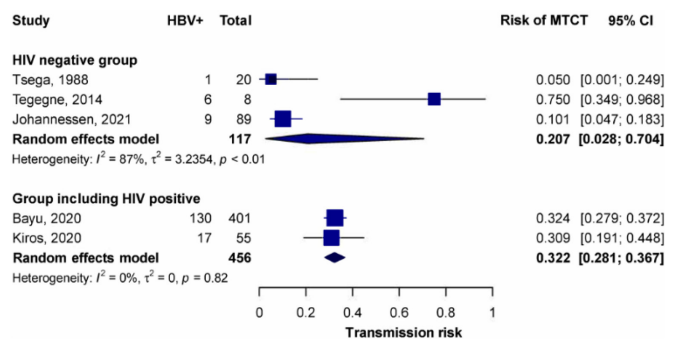
Figure 4 illustrates the risk of MTCT of HBV in HIV-positive and HIV negative women group after excluding an outlier study. One study was an outlier

with a risk of MTCT of HBV of 75.0%. After excluding this study, the subgroup analysis showed no heterogeneity between studies in both the subgroup including studies with HIV negative women ( $I^2 = 0, p = 0.48$ ) and the subgroup that included studies that studied women with HIV infection as well ( $I^2 = 0, p = 0.82$ ). The risk of MTCT of HBV in the HIV negative women group was 9.4% (95% CI 5.1%–16.6%).

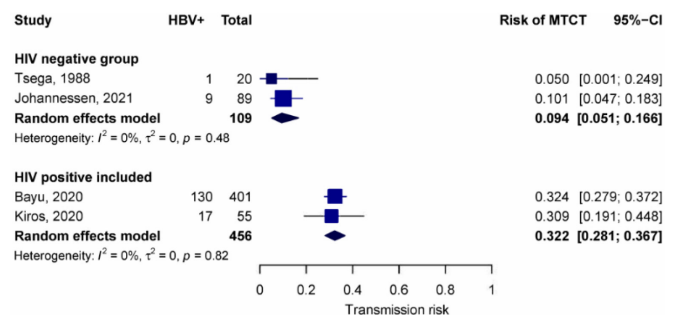
**Figure 2.** Overall pooled risk of mother-to-child transmission of hepatitis B virus in Ethiopia



**Figure 3.** Risk of mother-to-child transmission of HBV infection in studies that included only HIV negative women and studies including women with HIV infection, with all studies included.



**Figure 4.** Subgroup analysis of the risk of mother-to-child transmission of hepatitis B in studies that excluded HIV positive women and those that included HIV positive women after excluding an outlier study.



*Meta-regression*

In the mixed-effects meta-regression analysis, HIV status was a statistically significant factor associated with heterogeneity. Studies including HIV-positive women reported a higher proportion of vertical transmission of HBV compared with studies that included only HIV negative women ( $\beta = 0.48$ , 95% CI 0.21 - 0.75,  $p < 0.001$ ). HBeAg positivity rate was a source of heterogeneity with a higher proportion of women with HBeAg positive results associated with a higher rate of transmission ( $\beta = 0.5.81$ , 95% CI 2.14 – 9.47,  $p = 0.002$ ). The mean/median age of the mother also explained the heterogeneity ( $\beta = -0.86$ , 95% CI - 1.43 – -0.30,  $p = 0.003$ ) (Table 2).

**Discussion**

We conducted a systematic review and meta-analysis of the risk of MTCT of HBV in Ethiopia. Our analysis found that an estimated 25% of deliveries from mothers with HBV infection resulted in the transmission of HBV to their newborns. The risk of transmission was lower in studies conducted before the start of HIV epidemic in Ethiopia and in studies that excluded women with HIV infection (20.7%). The risk of MTCT was higher for the subgroup of studies that included women with HIV infection (32.2%). After excluding an outlier study, the pooled risk of MTCT of HBV in the group with all HIV negative women was 9.4%.

The MTCT risk for HBV in Ethiopia is high with an estimated 26% of HBV-exposed deliveries leading to HBV-infected newborns. This risk is of particular public health significance because of the higher prevalence of HIV infection in pregnant women than in the general population in Ethiopia [4], which is known to increase the risk of acquiring HBV infection in infants exposed to the hepatitis virus [22]. Despite the availability of immunoglobulin for exposed infants and antiviral prophylaxis during pregnancy in the global market, the high proportion of children born with HBV infection signals a considerable healthcare access gap that requires attention from the health system. The HIV endemic problem [10] coupled with resource constraints to scale up antenatal antiviral prophylaxis,

and implement immunoprophylaxis are critical factors that contribute to the perpetuation of childhood HBV infection and impede progress towards the control and subsequent elimination of HBV in Ethiopia. Unless additional preventive measures such as immunoglobulin prophylaxis are implemented, and existing interventions such as third-trimester antiviral prophylaxis strengthened, Ethiopia will see the vertical transmission of HBV from the mother to the newborn continue into the foreseeable future at such high rates due to the presence of HIV infection.

The pooled estimate of the risk of MTCT of HBV in Ethiopia might be influenced by the small sample size of included studies [20], which may provide an unstable estimate of the rate of MTCT of HBV. After excluding the study with the smallest sample size and highest risk of MTCT of HBV, the pooled risk for the subgroup became lower and the heterogeneity between studies was reduced to zero in the group with studies including only HIV negative women. In the meta-regression analysis, HIV positivity rate, HBeAg positivity rate, and age of the mother explained the heterogeneity between studies.

Compared with the risk reported from high prevalence countries such as in Asia [23], the risk of MTCT of HBV in Ethiopia is lower, like the rate in other African countries, which may be attributed to the low HBeAg positivity rate in this region. The low risk of transmission could also be due to geographic variations in the mode of transmission of HBV between Africa and Asia [24]. This level of risk is similar to earlier reports from studies in sub-Saharan African countries that showed a lower risk of transmission for Africa compared with other regions [24]. Given the high prevalence of HBV in Ethiopia and the high risk of vertical transmission, there is still a high likelihood that this route of infection continues to significantly contribute to the burden of chronic HBV in Ethiopia.

The lower risk of MTCT of HBV compared to reports from Asian countries might be partly explained by the fact that three studies did not include women with HIV infection, either due to negative tests in all women [20], or were excluded from the study [18]. Including only HIV negative mothers in some of the

**Table 2.** Mixed-effects meta-regression result for study-level predictors of heterogeneity.

Variable	Estimate	Standard error	95% Confidence interval		p value
			lower	upper	
HIV positivity rate	0.48	0.14	0.21	0.75	< 0.001 ***
HBeAg positivity status	5.81	1.87	2.14	9.47	0.002 **
Age of mother	-0.86	0.29	-1.43	-0.30	0.003 **
Intercept	17.18	6.76	3.93	30.43	0.011 *

Significance: \*\*\*, 0.001; \*\*, 0.01; \*, 0.05.

studies might have resulted in a lower pooled estimate of the risk of MTCT of HBV. The other reason might be because of the timing that some studies were conducted before the HIV epidemic began in Ethiopia which is known to increase the risk of vertical transmission [21].

Mother-to-child transmission of HBV has a more significant clinical relevance than just increasing the burden of chronic HBV because most (> 90%) infections progress to chronic HBV [7] and the clinical sequelae including liver fibrosis, cirrhosis, and hepatocellular carcinoma are associated with chronic infection [25]. It is, therefore, clinically sound and is a pragmatic public health approach that prevention of MTCT of HBV is a cost-effective strategy that reduces HBV burden, hospitalizations, and mortality from HBV-associated advanced liver diseases.

The progress towards elimination of MTCT of HBV in Ethiopia has been negatively impacted by the lack of adequate implementation and rollout of birth-dose HBV vaccination [26], and the absence of immunoglobulin prophylaxis [27]. Moreover, the high prevalence of HIV in pregnant women means MTCT of HBV remains important. Despite its worldwide expansion and proven effectiveness to prevent vertical transmission of HBV, most pregnant women in Ethiopia did not have access to third-trimester antiviral prophylaxis [19,20], which demonstrates a missed opportunity by the health system to protect newborns from acquiring infection.

In the context of limited health resources, integration of prevention of MTCT of HBV with well-established antenatal care and prevention of MTCT of HIV programs may provide a cost-effective alternative to rollout interventions targeting the prevention of vertical transmission of HBV. Integrated approaches with existing health services such as HIV prevention programs have been shown to solve the problem of healthcare access as these programs were scale-up universally with a wider reach [28,29]. Studies highlighted targeted healthcare interventions that adapt to the health needs of the local, at-risk populations could enhance efforts towards HBV elimination in those at risk and in the general population [30]. The strong program for the prevention of MTCT of HIV infrastructure and the presence of trained personnel in Ethiopia could be an opportunity to implement onsite HBV testing and treatment initiation as well as monitoring of treatment adherence during antenatal care [29,31,32]. Utilizing this established system will also provide opportunities for task-shifting of HBV testing and care to simplify HBV treatment and ensures

that a program is a sustainable approach in the context of limited resources [33,34]. The benefits of decentralizing viral hepatitis care to improve testing and treatment uptake rates, thereby accelerating the effectiveness of control programs are documented in other settings worldwide [35,36].

This is the first study that provided a national-level estimate of the risk of MTCT in Ethiopia, with a sample of 573 HBV-exposed deliveries. The study also examined and reflected on the shortcomings in the assessments of risk factors and prevention interventions and their impact on the risk of MTCT of HBV. However, there are several limitations of this study. First, there were a small number of studies that assessed MTCT of HBV and it was not methodologically possible to do meta-regression analysis to identify study-level factors that contributed to the heterogeneity. Subsequently, we explored the heterogeneity by undertaking a random-effects meta-analysis and doing a subgroup analysis based on HIV status (a known risk factor that increases the risk of MTCT of HBV). Another limitation of the study is that not all studies included women with risk factors known to affect the vertical transmission of HBV such as HIV infection and there was high heterogeneity as a result.

## Conclusions

The high risk of MTCT of HBV in Ethiopia with a disproportionately higher risk for children born to women with HIV infection shows a gap in access to testing and prophylaxis. In the context of HIV endemicity and limited resources to scale-up antiviral prophylaxis, MTCT of HBV will persistently contribute to the high burden of HBV-related morbidity and mortality in Ethiopia. There is a need for simplifying access to preventive services. Integrated approaches with existing HIV prevention services may provide opportunities for optimal utilization of scarce resources to narrow the access gap in immunoglobulin, and third-trimester antiviral prophylaxis to the mother and the newborn in Ethiopia.

## Authors' contributions

Belaynew Taye was involved in the concept and design of the study. Belaynew Taye and Eden Bishaw extracted the data and performed the analysis. Belaynew Taye drafted the manuscript and updated subsequent versions. Belaynew Taye, Girum Ayenew, Zewdu Wasie, Melashu Balew, and Eden Bishaw performed the analysis, wrote the manuscript and revised it for its intellectual content. All the authors read the final version of the manuscript and approved it for submission.

## References

- Gomaa AI, Khan SA, Toledano MB, Waked I, Taylor-Robinson SD (2008) Hepatocellular carcinoma: epidemiology, risk factors and pathogenesis. *World J Gastroenterol* 14: 4300-8. doi: 10.3748/wjg.14.4300.
- World Health Organization (WHO) (2021) Hepatitis B. Key facts. Available: <https://www.who.int/news-room/factsheets/detail/hepatitis-b>. Accessed: 11 October 2021.
- Yazie TD, Tebeje MG (2019) An updated systematic review and meta-analysis of the prevalence of hepatitis B virus in Ethiopia. *BMC Infect Dis* 19: 917. doi: h10.1186/s12879-019-4486-1.
- Tanga AT, Teshome MA, Hiko D, Fikru C, Jilo GK (2019) Sero-prevalence of hepatitis B virus and associated factors among pregnant women in Gambella hospital, Southwestern Ethiopia: facility based cross-sectional study. *BMC Infect Dis* 19: 602. doi: 10.1186/s12879-019-4220-z.
- Piratvisuth T (2013) Optimal management of HBV infection during pregnancy. *Liver Int.* 33: 188-94. doi: 10.1111/liv.12060.
- Ministry of Health Ethiopia (2020) Expanded Program on Immunization (EPI) Available: <https://www.moh.gov.et/ejcc/am/EPI>. Accessed: 11 October 2021.
- Fattovich G (2003) Natural history and prognosis of hepatitis B. *Semin Liver Dis* 23: 47-58. doi: 10.1055/s-2003-37590.
- Indolfi G, Easterbrook P, Dusheiko G, Siberry G, Chang MH, Thorne C, Bulters M, Chan PL, El-Sayed MH, Giaquinto C, Jonas MM, Meyers T, Walsh N, Wirth S, Penazzato M (2019) Hepatitis B virus infection in children and adolescents. *Lancet Gastroenterol Hepatol* 4: 466-476. doi: 10.1016/S2468-1253(19)30042-1.
- Taye BW, Clark PJ, Hartel G, Powell EE, Valery PC (2021) Remoteness of residence predicts tumor stage, receipt of treatment, and mortality in patients with hepatocellular carcinoma. *JGH Open* 5: 754-762. doi: 10.1002/jgh3.12580.
- Kassa D, Gebremichael G, Tilahun T, Ayalkebet A, Abrha Y, Mesfin G, Belay Y, Demissie M, Gebrexiabher A, Assefa Y (2019) Prevalence of sexually transmitted infections (HIV, hepatitis B virus, herpes simplex virus type 2, and syphilis) in pregnant women in Ethiopia: Trends over 10 years (2005-2014). *Int J Infect Dis* 79: 50-57. doi: 10.1016/j.ijid.2018.11.009.
- Atalay AA, Abebe RK, Dadhi AE, Bededa WK (2021) Seroprevalence of hepatitis B virus among pregnant women attending Antenatal care in Dilla University Referral Hospital Gedio Zone, Ethiopia; health facility based cross-sectional study. *PLoS One* 16: e0249216. doi: 10.1371/journal.pone.0249216.
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 6: e1000097. doi: 10.1136/bmj.b2535.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, Mcdonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372: n71. doi: 10.1136/bmj.n71. doi: 10.1136/bmj.n71.
- Wells GA, Wells G, Shea B, O'Connell D, Peterson J, Welch, Losos M (2012) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa, Ontario, Canada: Ottawa Hospital Research Institute.
- Modesti PA, Reboldi G, Cappuccio FP, Agyemang C, Remuzzi G, Rapi S, Perruolo E, Parati G; ESH Working Group on CV Risk in Low Resource Settings (2016) Panethnic differences in blood pressure in Europe: A systematic review and meta-analysis. *PLoS One* 11: e0147601. doi: 10.1371/journal.pone.0147601.
- Geissbühler M, Hincapié CA, Aghlmandi S, Zwahlen M, Jüni P, da Costa BR (2021) Most published meta-regression analyses based on aggregate data suffer from methodological pitfalls: a meta-epidemiological study. *BMC Med Res Methodol* 21: 123. doi: 10.1186/s12874-021-01310-0.
- Bayu H, Elias B, Abdisa S, Tune A, Namoh H (2020) Post-exposure prophylaxis coverage, vertical transmission and associated factors among hepatitis B exposed newborns delivered at Arsi zone health institutions, 2019. *Plos One* 15: e0238987. doi: 10.1371/journal.pone.0238987.
- Johannessen A, Mekasha B, Desalegn H, Abera H, Stene-Johansen K, Berhe N (2021) Mother-to-child transmission of hepatitis B virus in Ethiopia. *Vaccines (Basel)* 9: 430. doi: 10.3390/vaccines9050430.
- Kiros KG, Goyteom MH, Tesfamichael YA, Mekonen HH, Gebru TH, Gebrehiwot TG, Teka YH, Abrha WA, Tadesse DB (2020) Seroprevalence of Hepatitis B virus infection, mother-to-child transmission, and associated risk factors among delivering mothers in Tigray Region, Northern Ethiopia: a cross-sectional study. *Infect Dis Ther* 9: 901-911. doi: 10.1007/s40121-020-00340-3.
- Tegegne D, Desta K, Tegbaru B, Tilahun T (2014) Seroprevalence and transmission of Hepatitis B virus among delivering women and their newborn in selected health facilities, Addis Ababa, Ethiopia: a cross-sectional study. *BMC Res Notes* 7: 239. doi: 10.1186/1756-0500-7-239.
- Tsega E, Tsega M, Mengesha B, Nordenfelt E, Hansson BG, Lindberg J (1988) Transmission of hepatitis B virus infection in Ethiopia with emphasis on the importance of vertical transmission. *Int J Epidemiol* 17: 874-9. doi: 10.1093/ije/17.4.874
- Chotun N, Nel E, Cotton MF, Preiser W, Andersson MI (2015) Hepatitis B virus infection in HIV-exposed infants in the Western Cape, South Africa. *Vaccine* 33: 4618-4622. doi: 10.1016/j.vaccine.2015.06.076
- World Health Organization. Regional Office for the Western Pacific (2006) Preventing mother-to-child transmission of hepatitis B: operational field guidelines for delivery of the birth dose of hepatitis B vaccine. WHO Regional Office for the Western Pacific. Available: <https://apps.who.int/iris/handle/10665/272905>. Accessed: 11 October 2021.
- Keane E, Funk AL, Shimakawa Y (2016) Systematic review with meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa. *Aliment Pharmacol Ther* 44: 1005-1017. doi: 10.1111/apt.13795.
- Yang JD, Mohamed EA, Aziz AO, Shousha HI, Hashem MB, Nabeel MM, Abdelmaksoud AH, Elbaz TM, Afihene MY, Duduyemi BM, Ayawin JP, Gyedu A, Lohouès-Kouacou MJ, Ndam AW, Moustafa EF, Hassany SM, Moussa AM, Ugiagbe RA, Omuemu CE, Anthony R, Palmer D, Nyanga AF, Malu AO, Obekpa S, Abdo AE, Siddig AI, Mudawi HM, Okonkwo U, Kooffreh-Ada M, Awuku YA, Nartey YA, Abbew ET, Awuku NA, Otegbayo JA, Akande KO, Desalegn HM,

- Omonisi AE, Ajayi AO, Okeke EN, Duguru MJ, Davwar PM, Okorie MC, Mustapha S, Debes JD, Ocama P, Lesi OA, Odeghe E, Bello R, Onyekwere C, Ekere F, Igetei R, Mah'moud MA, Addissie B, Ali HM, Gores GJ, Topazian MD, Roberts LR, Africa Network for Gastrointestinal and Liver Diseases (2017) Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium. *Lancet Gastroenterol Hepatol* 2: 103-111. doi: 10.1016/S2468-1253(16)30161-3.
26. World Health Organization (2017) Global hepatitis report 2017. World Health Organization, Geneva, Switzerland. Available: <https://apps.who.int/iris/handle/10665/255016>.
  27. Federal Democratic Republic of Ethiopia Ministry of Health (2015) Health Sector Transformation Plan (2015/16-2019/20). Federal Ministry of Health, Addis Ababa, Ethiopia.
  28. Cohn J, Owiredun MN, Taylor MM, Easterbrook P, Lesi O, Francoise B, Broyles LN, Mushavi A, Van Holten J, Ngugi C, Cui F, Zachary D, Hailu S, Tsiouris F, Andersson M, Mbori-Ngacha D, Jallow W, Essajee S, Ross AL, Bailey R, Shah J, Doherty MM (2021) Eliminating mother-to-child transmission of human immunodeficiency virus, syphilis, and hepatitis B in sub-Saharan Africa. *Bull World Health Organ* 99: 287-295. doi: 10.2471/BLT.20.272559.
  29. Thompson P, Morgan CE, Ngimbi P, Mwandagalirwa K, Ravelomanana NLR, Tabala M, Fathy M, Kawende B, Muwonga J, Misingi P, Mbendi C, Luhata C, Jhaveri R, Cloherty G, Kaba D, Yotebieng M, Parr JB (2021) Arresting vertical transmission of hepatitis B virus (AVERT-HBV) in pregnant women and their neonates in the Democratic Republic of the Congo: a feasibility study. *Lancet Glob Health* 9: e1600-e1609. doi: 10.1016/S2214-109X(21)00304-1.
  30. Taye BW, Valery PC, Clark PJ (2022) Targeted antiviral treatment of hepatitis B virus in culturally and linguistically diverse populations to achieve elimination targets in Australia. *J Viral Hepat* 29: 868-878. doi: 10.1111/jvh.13727.
  31. Wilson P, Parr JB, Jhaveri R, Meshnick SR (2018) Call to action: prevention of mother-to-child transmission of hepatitis B in Africa. *J Infect Dis* 217: 1180-1183. doi: 10.1093/infdis/jiy028.
  32. Andersson MI, Rajbhandari R, Kew MC, Vento S, Preiser W, Hoepelman AI, Theron G, Cotton M, Cohn J, Glebe D, Lesi O, Thursz M, Peters M, Chung R, Wiysonge C (2015) Mother-to-child transmission of hepatitis B virus in sub-Saharan Africa: time to act. *Lancet Glob Health* 3: e358-9. doi: 10.1016/S2214-109X(15)00056-X.
  33. Taye BW (2019) A path to ending hepatitis C in Ethiopia: A phased public health approach to achieve micro-elimination. *Am J Trop Med Hyg* 101: 963-972. doi: 10.4269/ajtmh.19-0295.
  34. Hellard M, Howell J (2022) Simplify access to hepatitis B care. *Nature* 603: S53-S53. doi: 10.1038/d41586-022-00815-y.
  35. Oru E, Trickey A, Shirali R, Kanters S, Easterbrook P (2021) Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. *Lancet Glob Health* 9: e431-e445. doi: 10.1016/S2214-109X(20)30505-2.
  36. Tran L, Feldman R, Riley T III, Jung J (2021) Association of the extension for community healthcare outcomes project with use of direct-acting antiviral treatment among US adults with hepatitis C. *JAMA Netw Open* 4: e2115523. doi: 10.1001/jamanetworkopen.2021.15523.

#### Corresponding author

Dr Belaynew Taye, MD, MPH, PhD  
 Postdoctoral Researcher – Infectious Disease Epidemiology  
 Wesfarmers Centre of Vaccines and Infectious Diseases  
 Telethon Kids Institute  
 15 Hospital Avenue, Northern Entrance Perth Children's Hospital  
 6053 Nedlands, Perth, Australia  
 Tel: +61478064465  
 Email: [belaynew.taye@telethonkids.org.au](mailto:belaynew.taye@telethonkids.org.au); [bewassie@gmail.com](mailto:bewassie@gmail.com)

**Conflict of interests:** No conflict of interests is declared.



**Annex – Supplementary Items****Supplementary Table 1.** Detailed search terms for all databases searched.

Database	Search terms
PubMed	((hepatitis B[Title/Abstract]) AND ('mother to child transmission'[Title/Abstract] OR 'vertical transmission'[Title/Abstract])) AND (Ethiopia[Title/Abstract] ""hepatitis b""[Title/Abstract] AND (""mother to child transmission""[Title/Abstract] OR ""vertical transmission""[Title/Abstract]) AND ""Ethiopia""[Title/Abstract])
EMBASE	"hepatitis b':ab,ti AND ('vertical transmission':ab,ti OR 'mother to child transmission':ab,ti) AND ethiopia:ab,ti"
Web of Science	((AB=(hepatitis B)) AND AB=(mother to child transmission OR vertical transmission)) AND AB=(Ethiopia)
Africa Index Medicus	(tw:(hepatitis B OR hepatitis b surface antigen)) AND (tw:(mother to child transmission OR vertical transmission)) AND (tw:(Ethiopia))

**Supplementary Table 2.** NOS Scale for Risk of Bias and Quality Assessment - Cross-Sectional Studies.

Study ID	Selection				Comparability	Outcome		Score
	Representativeness of the sample	Sample size	Ascertainment of exposure	Non-respondents	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.	Assessment of outcome	Was follow-up long enough for outcomes to occur	
Tsega <i>et al.</i>	*	*	*	*	*	*	*	11
Tegegne <i>et al.</i>	*		*		*	*	*	8
Kiros <i>et al.</i>	*	*	**	*	**	*	*	11
Bayu <i>et al.</i>	**	*	*	*	*	*	*	11
Johannessen <i>et al.</i>	**		**	*	*	*	*	10