

**DISSERTATION SUBMITTED FOR THE MASTER'S DEGREE IN
MEDICAL MICROBIOLOGY**



TITLE

**SEROPREVALENCE OF HEPATITIS E INFECTION AMONG
PREGNANT WOMEN AND CLINICAL FEATURES OF INFANTS
BORN TO HEV INFECTED MOTHER**

SUBMITTED BY

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**DEPARTMENT OF MICROBIOLOGY
INTEGRAL INSTITUTE OF MEDICAL SCIENCES & RESEARCH
INTEGRAL UNIVERSITY**

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A

DISSERTATION

Submitted to

INTEGRAL UNIVERSITY

In partial fulfillment of the requirements for the award of degree of



Masters of sciences

In

Medical Microbiology

By

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DECLARATION OF CANDIDATE

I hereby declare that this dissertation entitled **“SEROPREVALENCE OF HEPATITIS E INFECTION AMONG PREGNANT WOMEN AND CLINICAL FEATURES OF INFANTS BORN TO HEV INFECTED MOTHER ”** is bonafide and genuine research work carried out by me under the guidance of **Dr. NOOR JAHAN** Professor & HOD, Department of Microbiology and Co- guide **Dr. SIRAJ AHMAD** and **Dr. AUSAF AHMAD** Professor & Associate Professor, Department of Community Medicine, Integral Institute of Medical Sciences and Research, Lucknow.

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CERTIFICATION

This is to certify that the thesis entitled “**SEROPREVALENCE OF HEPATITIS E INFECTION AMONG PREGNANT WOMEN AND CLINICAL FEATURES OF INFANTS BORN TO HEV INFECTED MOTHER**” has been done and submitted by **MR BUHARI UMAR BACHA** with **ROLL NO. 1900104334** in partial fulfillment of the requirement for the award of degree of **MASTER OF MEDICAL MICROBIOLOGY** “ to the INTEGRAL UNIVERSUTY LUCKNOW during the session of 2019-2022 , under the supervision of **Prof [DR] NOOR JAHAN**, and co-guide **Prof [DR] SIRAJ AHMAD** and **DR AUSAF AHMAD**, he fulfill all the laid under the guidelines

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CERTIFICATE BY THE GUIDE & CO-GUIDE

This is to certify that the dissertation entitled **“SEROPREVALENCE OF HEPATITIS E INFECTION AMONG PREGNANT WOMEN AND CLINICAL FEATURES OF INFANTS BORN TO HEV INFECTED MOTHER”** is a bonafide and genuine research work done by **BUHARI UMAR BACHA** in partial fulfilment of the necessity for the degree of Masters of Science in Medical Microbiology.

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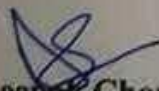
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CERTIFICATE

This is to certify that research work entitled "Seroprevalence of hepatitis E virus in pregnant women and clinical features of fetus born to HEV infected mother systematic review" submitted by **Buhari Umar Bacha, Dr.Noor Jahan, Dr.Siraj Ahmad, Dr.Ausaf Ahmad** for ethical approval before the Institutional Ethics Committee IIMS&R.

The above mentioned research work has been approved by Institutional Ethics Committee, IIMS&R with consensus in the meeting held on **19 May 2022**.


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BUHARI UMAR BACHA

DEDICATION

TO MY BEST EVER HUMANS WHOM WITHOUT

THEM NOTHING IS POSSIBLE

{MY PARENTS}

I LOVE YOU AND WOULD KEEP ON LOVING YOU

FOREVER

CONTENT

NOTATION	[1]
CERTIFICATION.....	[3]
ETHICAL CERTIFICATE	[8]
DECLARATION	[9]
COPYRIGHT DECLARATION	[10]
ACKNOWLEDGEMT	[11]
DEDICATION	[12]
INRTRODUCTION	[14]
LITRATURE REVIEW	[19]
METHOLOGY	[24]
DATA ANALYSIS	[28]
RESULT	[32]
OBSERVATION.....	[37]
REFRENCES	[39]

INTRODUCTION

A study in Cameroon by Bigna JJ et al stated that HEV is a water- and food-borne infection that can potentially cause acute outbreaks in populations with poor sanitation however, zoonotic and transfusion related transmission have also been documented, to date no specific treatment exists for HEV infection as a consequence, its management relies mostly on supportive care.

Systematic review study by Dagne M et al in Ethiopia mention that Hepatitis E virus (HEV), first recognized in Asia almost 38 years ago as the main cause of non-A, non-B enterically transmitted hepatitis and the only hepatitis virus that has animal reservoir, HEV is becoming an emerging infectious agent causing mainly acute infection worldwide and a major cause of epidemic water-borne hepatitis in tropical and subtropical countries.

Study in India by Chaudhry SA et al stating Hepatitis E infection during pregnancy and in the third trimester, especially with genotype {I} is associated with more severe infection in pregnant women and might lead to fulminant hepatic failure and maternal death although the mechanism of liver injury is not yet clear, it is possible that interplay of hormonal and immunologic changes during pregnancy, along with a high viral load of HEV, renders the woman more vulnerable.

Khuroo MS et al in observational study at J&K India find out that pregnant women especially in the second and third trimester develop FHF. The mortality in the second trimester is around 20% and reaches up to 45% in the third trimester; Hepatitis E Virus is also commonly transmitted from infected mother to the fetus and causes serious foetal and neonatal infections with significant foetal loss and perinatal morbidity and mortality.

A study by Salam GD et al in India suggest that Immune system in response to viral infection results in the production of many cytokines that act as mediators of disease activity i.e. [IL]-1&6 [TNF]-a TNF-a play an important role in mediating a series of

pregnancy events, The activation of some forms of maternal cellular immunity is potentially hazardous for the fetal development. Although largely a self-limiting infection, HEV results in morbidity and mortality, especially among pregnant women.

Jilani N et al in India mention that there is also a reduced level of immunity due to a marked reduction in T cells during early pregnancy up to the 20th week of gestation, Pregnancy is characterized by a transient depression of cell-mediated immunity in the woman that allows fetal allograft retention, but also interferes with resistance of the mother to various infectious diseases, Acute hepatitis E virus infection diagnosed by the detection of HEV-RNA or IgM & IgG anti-HEV antibodies.

Kim JH et al systematics review study in Africa, taking a particularly high toll in pregnant women and their fetuses, HEV has infected human populations in 28 of 56 African countries. Since 1979, 17 HEV outbreaks have been reported about once every other year from Africa causing a reported 35,300 cases with 650 deaths. HEV may develop into fulminant hepatitis with a case-fatality rate (CFR) between 1 and 2% in the general population which can rise to over 40% in pregnant women.

Kamili S et al in retrospective study at Kashmir India, the proportion of cases of sporadic AVH in pregnancy caused by HEV and other hepatitis viruses is not known. Whether hepatitis viruses other than HEV have increased incidence and severity in pregnancy in developing countries is also not known. How does FHF in pregnancy differ from those in non-pregnant women also this mechanism is yet unknown?

Aggarwal R et al in India, the most employed lab diagnostics procedure for HEV infection are isolation of IgM and IgG anti-HEV antibodies and detection of HEV RNA, IgM anti-HEV are detected in patient with current disease of HEV infection, whereas IgG anti-HEV antibodies represent either recent or previous exposure. HEV RNA [rtPCR] indicates current infection whether acute or chronic and its confirmation of antibody test.

Study in India by Satsangi S et al, numbers of HEV epidemic infection often occur in India ranges from the year 1955 to 2008 at various Indian locality and infect around one hundred and fifty individual at various time of the epidemic, During the epidemic the

secondary attack rate among the household contacts is estimated to be about 0.7–2% and infected pregnant women mostly developed acute liver failure.

A systematic review study by H. C LEWIS et al [CAMBRIDGE UNIVERSITY USA 2009] identified major potential risk factor and route of transmission in HEV infection which include age and sex factor, potential zoonotic transmission by direct contact, potential foodborn zoonotic factor, potential transmission through human sewage, potential water born transmission, potential parental transmission, comorbidity transmission factor like diabetes hypertension or compromised immune.

A study in Europe by Walter M et al stating Within the first 3 days of clinical illness with jaundice and elevated aminotransferases (ALT), HEV igM & IgG both is detectable in 71% of blood and 60% By the end of the first week , HEV virus is also shed in feces up to 1 month after onset of illness, while present at first week in some patient by 6weeks of onset almost HEV viremia is cleared and HEV IgM is mostly in few patient while HEV IgG can still be detectable in nearly all the patients,

The level of liver enzyme AST circulated in pregnant women blood particularly HEV IgM positive is (40–20 IU/L) this was double than that in general population which is (<20 IU/L). This suggest pregnant women in their third trimester of pregnancy are more susceptible to HEV infection and may cause more severe liver damage or lesions of the liver this may account an extremely high chance of mortality rate in their third trimester of pregnancy.

An observational study conducted in LOK NAYAK HOSPITAL DELHI INDIA by Syed A. Husain, Ph.D., Et al suggest there is very high rate of HEV infection in pregnant FHF patients (38/50, 76%) when compared with those of non-pregnant FHF 2499 patients (17/50, 34%;P<0.05) 38

It's common throughout pregnancy more especially during third trimester when levels of sex steroid hormones are high; viruses are much likely to replicate and spread rapidly, reaching high titers in tissues and produce more and severe disease

LITERATURE REVIEW

A study by [H. JIN, Y. ZHAO, X. ZHANG, B. WANG et al. March 2016] A total of 4306 titles and abstracts screened then 135 full articles were retrieved. The study indicate that women in the third trimester had a higher CFR compare to 1st & 2nd, and intrauterine fetal mortality is (27.0%) which is statistically higher than neonatal mortality as reported at (3.9%) in pregnant women infected with AHE this is due to fact that AHE infection is much common in 3rd trimester of pregnancy and severe maternal condition bring about pregnancy termination, which results in intrauterine fetal death or premature births, Some studies show that worsening of HEV condition in mother and baby may typically related and that fetal disease influences the course of maternal HEV infection.*

HAV and HEV which are fecal-oral transmission mainly present as acute hepatitis during pregnancy and are responsible for most local epidemic outbreaks, although HAV infection is self-limiting in pregnancy, but HEV has higher prevalence and causes significant morbidity, It is also associated with extreme high maternal mortality rate, WHO estimates that about 20 million new HEV infections worldwide was recorded, causing 3.3 million symptomatic cases of hepatitis E, resulting in 44 000 deaths in 2015, this accounting for 3.3 % of the mortality due to viral hepatitis

A retrospective study by M.S KHUROO & S. KAMILI [Nov 2008] include 26 pregnant women with HEV infection, one was in first trimester, five in second trimester and 20 in third trimester. Fifteen (57.7%) mothers had developed FHF. Of these, 12 presented with clinical features of FHF and another three developed FHF during the hospital course. Nine (60.0%) of the 15 mothers with FHF died and 6 (40.0%) survived, Fifteen (78.9%) babies at birth revealed evidence of HEV infection seven babies died in the first week of birth Nine HEV infected babies survived

A study by [Anne Bergløv] et al University of Copenhagen, Denmark, show a high CFR among pregnant women infected with hepatitis E virus with extreme chances of maternal and neonatal adverse outcomes in relation to the infection. More of those who have severe complications like FHF. However, the case-fatality rate might be overestimated due to the inclusion of mainly symptomatic women.¹¹

In a prospective study by RAHUL KARNA et al. [Oct 2019] at Lok Nayak hospital Delhi included 1088 patients were 550 pregnant were 411 patients with AVH and 139 patients with ALF and 538 non pregnant were 357 patients with AVH and 181 patients with ALF. HEV infection was observed in 82.72% (340/411) of AVH pregnant group but in only 43.41% (155/357) of cases in the AVH non pregnant group. In the ALF cases, the prevalence of HEV was observed in 73.38% (102/139) in the pregnant group and 61.32% (111/181) in non-pregnant group. Ninety-eight of 129 (75.96%) cases of HEV-infected pregnant women died, whereas non-HEV infection was responsible for only 31 of 129 (24.04%) cases' death in comparison

A study by Robert A. de Man et al show In 2005, it was estimated that HEV genotypes 1 and 2 were responsible for about 20.1 million incidents of HEV infections, 3.4 million symptomatic cases, 70 000 fatalities, and 3000 stillbirths.

The pooled seroprevalence of HEV among pregnant women in African continent is estimated as 29.13%, Egypt is reported highest seroprevalence of 84.3% and Gabon with 6.6% the lowest rate, Ghana 28.6% and central Africa with 33%

A cross sectional study carryout in Nigeria [university of Maiduguri] by Ibrahim Musa Kida et al[2020] show that pregnant women in third trimester had highest seroprevalence of anti-HEV IgM, 14.1%. then those in second trimester, 12.8% and lowest is seen in women of first trimester, A recent study in Nigeria both meta-analysis and systematic review show a pooled HEV prevalence estimated at 10.8% and 65.7% in other population, infection in pregnant women, however is associated with increased risk of childbearing conditions such as abortion, stillbirth, low birth weight and preterm labor

A study carryout mainly in south western Nigeria by Adesina, O. A. et al [2021] report a high seroprevalence of 36.5% in four state and 0.4% among pregnant women at ekiti lagos osun and oyo state respectively

A study by Adeola Fowotade, et al [2020] at college of medicine university of Ibadan Nigeria involve 230 asymptomatic pregnant women from difference child bearing ages which indicate HEV IgM antibodies detected in 11 (4.8%) while HEV IgG antibodies was detected in 39 (17.0%). None of the HEV IgM-positive participants was positive for HEV IgG antibodies. Of the 11 HEV IgM-seropositive women, three (27.3%) were confirmed positive for HEV RNA by PCR. All the 11 stool samples were negative for HEV RNA [17](#)

Cross sectional study by Surajudeen A. Junaid et al [2014] at plateau northern Nigeria analyze different mode of HEV transmission in the region and case fatality rate which indicate that animals handlers especially pigs are more at risk of getting infection since animals may be the reservoir of the infection also show that people in rural area are more prone than who are in urban area

In India and Indian subcontinent study show that more than 70% of acute hepatitis occurring in pediatrics population are caused by HEV and 80% are sporadic infection were mostly around 90% are enterically transmission and 5% are maternal-neonatal transmission

An observational study by Valsan Philip Et Al [2014] Most HEV infections in endemic areas are due to enteral transmission, usually due to fecal contamination of drinking water. Parenteral transmission of HEV through blood transfusion has also been documented, and HEV transmission from mother to infant, HEV has been found in domestic and wild pigs worldwide and increased anti-HEV sero positivity in pig handlers and swine veterinarian study also suggest that pigs can act as reservoirs of HEV in nonendemic countries.

In developed countries the rate is significantly low. A study by Lindemann *et al* [Spain] about 1040 pregnant women included in the study and reported the rate of anti-HEV IgG

is 3.6%. Prevalence of HEV IgG also found to be 7.7% and 10% in pregnant women in France and China, respectively

During a 2010–2011 outbreak in Sudan, 14 intrauterine deaths and 9 premature deliveries were reported among 39 pregnant hepatitis E cases. To date, only hepatitis E caused by HEV genotype 1 has consistently been observed to yield these effects in pregnancy

METHODOLOGY

Study protocol

An extensive and inclusive search was carryout from Dec 2021 to Feb 2022, were I performed a systematic search for the published articles on hepatitis E virus infection in pregnant women, cross transmission of HEV, outcomes of baby born to HEV infected mother. Specific and clear criterions were setup while conducting the search. The entire process was in accordance's with ' PRISMA' guidelines [preferred reporting items for systematic review and meta-analysis]

STUDY SELECTION

Study published up to Feb 2022 on HEV infection in pregnancy, cross transmission of HEV, outcome of fetus born to HEV infected mother those published around the world were included, only studies published in English were included meanwhile there is no age restriction. Exclusion were duplicate, books chapter, review, published articles on HEV infection not related to pregnancy and other irrelevant studies. Some studies were not accessible due to policy or monetization issues and effort have been made to contact the owner

ARTICLES SEARCH STRATEGIES

A comprehensive search was carryout in PubMed, Science Direct, Web of science, Scopus and Research Gate Database, using keywords: hepatitis e virus AND pregnancy OR pregnant women THEN maternal transmission of HEV AND seroprevalence of HEV and some search were made manually

OUTCOMES

FIG: B1: Prisma flow chat describes procedure of literature selection; a number of 3557 articles were identified from the above mention database respectively, and also some articles are collected by screening references which amount to 7 articles, after removing duplicate the number of articles comes to 1061. Out of 1061 articles I then synthesized 24 original research articles those provide relevant information while 1045 articles also excluded for the following reasons:

- 1: Non hepatitis E articles i.e. ABC {n=551}*
- 2: Non-pregnant women population [n=204]*
- 3: Non English articles [n= 139]*
- 4: Review articles [89]*
- 5: insufficient information [mostly case report] [17]*
- 6: Book chapter [25]*
- 7: result with unclear source and result [15]*

The seroprevalence were calculated using formula.

Seroprevalence (%) = HEV infected women /Total number of pregnant women

Seroprevalence was define as ‘the presence of anti-HEV antibody (IgG) in the plasma/ serum of pregnant women by the ELISA method’. [26]

Source and data extraction

Out of 24 included studies 14 articles are of seroprevalence the data come from Nigeria [n=2] India [n=7] China [N=2] Ethiopia [n=1] Iran [n=1] Ghana [n=1] Africa [n=1] and neonates outcomes born to HEV infected mother amount for 4 studies the data were all came from India [n=5]and remaining 4 studies are of case fatality rate among HEV infected mother and their fetus which come from India [n=2]Nigeria [n=1] UAE [n=1]

I were extract the data from included studies independently and the following information were extracted for each selected study,

Author last name(s), country, publication year, study design, sample size, anti-HEV antibody (IgG and IgM), and anti-HEV antibody detection method, data then entered into Microsoft Excel 2010

Fetal death due to maternal death and still-birth (defined as an infant born with no signs of life at or after 20 weeks of gestation [23])

Neonatal death was defined as live born infants who died within the first weeks of life; Vertical transmission was defined as blood samples collected from the infant within two weeks of birth with detectable IgM anti-HEV or HEV RNA [24]

,

FIG: B1

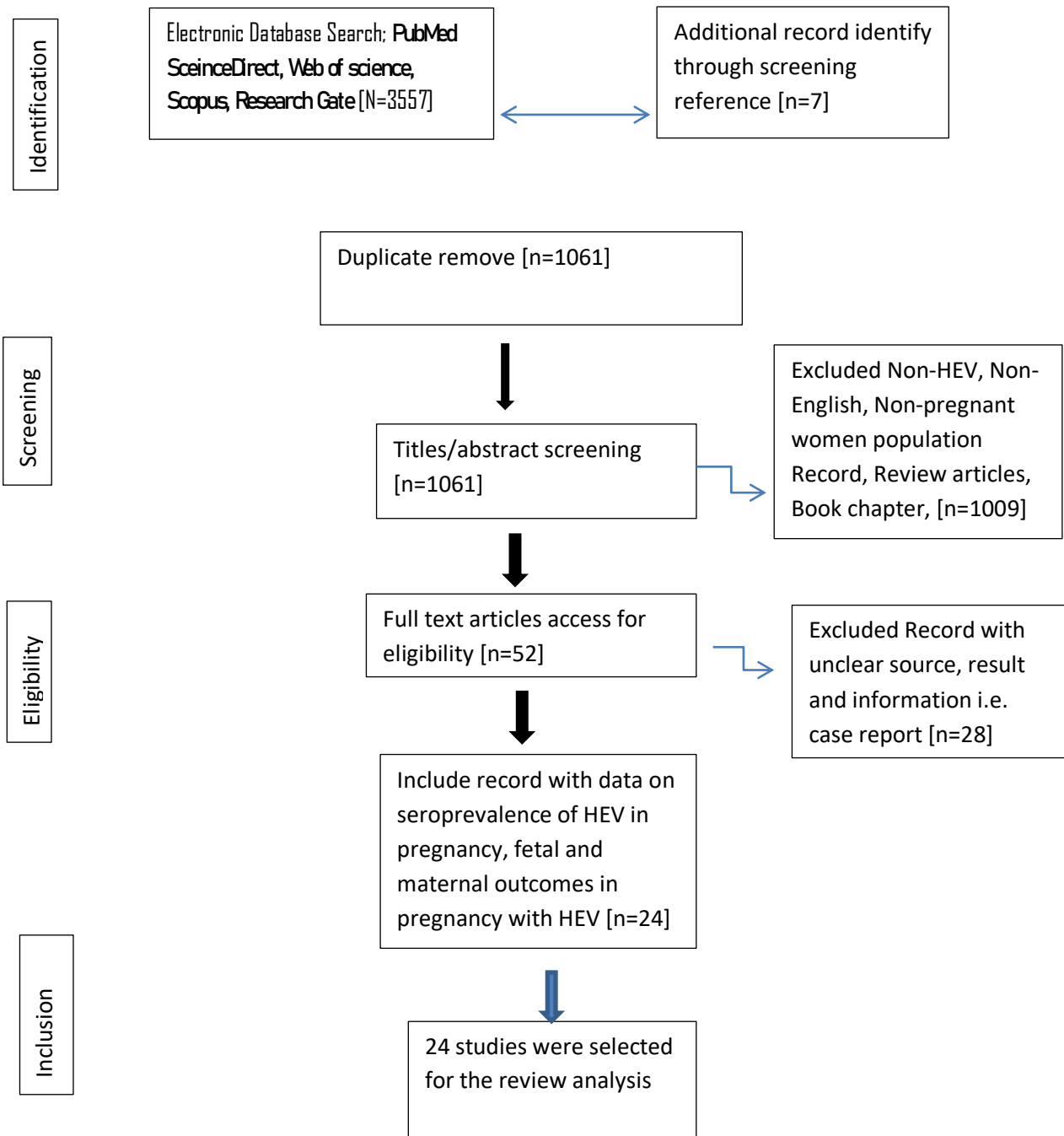


FIG: B1. **PRISMA CHART FOR INCLUSION AND EXLUSION CRITERA**

RESULT

An extensive and collective strategic search were made on internet using appropriate terms at specific database in which 3557 articles are retrieve, these articles undergo a wide screening were 24 search report found eligible for this study accordingly, of 24 studies, 14 report seroprevalence of HEV infection among pregnant women and 6 studies report fetal outcomes born to HEV infected mother while remaining 4 studies report case fatality rate of both mothers and their neonates.

Seroprevalence

A study conducted in India report high prevalence of HEV infection among pregnant women attending hospital in Kashmir India [81.5%] though this research employed a limited sample size of 90 subject were high mortality rate also recorded in this study from both mothers and theirs neonates⁸ while study conducted in Nigeria from 2016 to 2017 report a very low seroprevalence of HEV IgG antibodies among pregnant women attending antenatal care clinical with [9.9%]³⁴ another study carryout in northern Nigeria between 2015 to 2016 also report an average low HEV IgG antibodies seroprevalence among pregnant women with [13.3%]¹⁵. Africa being considered as a undeveloped region with a high risk and chance of developing different infectious and communicable disease due to level of poverty, lack of access and non-equipped health system still recorded a low seroprevalence of HEV infection among pregnant women according to report included in this studies, one systemic review study conducted in Africa report a very low HEV IgG seroprevalence in pregnant women from almost African country with overall pool seroprevalence of [15.9%]² One observational sampling study conducted in Ghana around 2008 at Accra teaching hospital report a low HEV IgG seroprevalence among pregnant women amount of [28.6%]³⁵ another study from Ethiopia report [32.11%]²⁹ which is slightly high but this study report a very low fatality rate of infection both in mother and their neonates, study conducted in republic of Iran report [4.7%]²⁸ which recorded most

lowest among the included articles, two study from Republic of China also report an average low HEV IgG seroprevalence among pregnant women with [18.8%]³⁰ , then one study conducted primarily for Chinese pregnant women in their third trimester report [24.8%]²⁵ this study was carryout between 2011 to 2015 which suggest pregnant women in their third trimester are highly susceptible to HEV infection. One study conducted in India reported a low HEV IgG seroprevalence among pregnant women with [19%]⁶ which is the lowest among included study from India were most of the Indian studies included in this research report a high or average high HEV IgG antibodies seroprevalence in pregnant women and all the study come from diverse locality of India, Two study both from India report around 50%, a high seroprevalence of HEV IgG among pregnant women, one study report [48.8%]³⁸ and another study conducted around 2017 to 2018 in India report [48%]⁴⁵ this study also found significantly higher mortality rate in HEV-infected pregnant women (25/38; 65.8%) than in HEV-infected non pregnant ones (4/17; 23.5%)($P < 0.0\%$). In another hospital base study conducted around 2010 to 2011 in India report a high HEV IgG antibodies seroprevalence among pregnant women with [40%]⁴³, another recent study conducted in India from 2018 to 2019 show significant decrease in seroprevalence of HEV IgG among pregnant women in India this study report [33.6%]²⁸. Fig: B2 represent characteristic of the included studies for seroprevalence of HEV infection among pregnant women

FIG: B2

s/no	Study	Year	Sampling year	Country	Sample size	HEV positive- [%]	Age...	Study type	Ref
1	Kanarkoohi	2021	2018-2019	Republic of Iran	420	20 - 4.7%	19-45	OSB	27
2	Dagnew	2019	2018	Africa	7921	1263-15.9%	13-49	SR	2
3	Begum N	2019	2018-2019	India	300	33.77%	---	HB	28
4	Ibrahim Ali	2017	2014-2015	Ethiopia	386	124-32.1%	16-40	CS	29
5	Wei long	2014	2011-2013	China	990	18.8%	18-43	CS	30
6	Ajayi BB	2022	2016	Nigeria	180	13.3%	-----	CS	15
7	Bello	2017	2016	Nigeria	182	18-9.9%	-----	CS	34
8	Adjei	2009	2008	Ghana	157	45-28.6%	13-42	OBS	35
9	Fen Huang	2015	2011-2015	China	274	68-24.8%	17-43	CS	25
10	Premashir Kar	2017	2018	India	125	60-48%	14-45	CPS	38
11	MS khuroo	2003	2002	India	76	65-81.5%	15-46	CS	8
12	Singh	2011	2010	India	50	20-40%	13-40	HB	43
13	Prabi	2014	2008-2011	India	90	44-48.8%	----	CS	45
<u>14</u>	<u>Nishat Jilani</u>	<u>2007</u>	<u>---</u>	<u>India</u>	<u>200</u>	<u>38-19%</u>	<u>19-45</u>	<u>OBS</u>	<u>6</u>

FIG: B2; Characteristic of included study for seroprevalence of HEV in pregnant women

Abbreviation

HB= Hospital based study

CS= Cross sectional study

OBS= Observational study

CPS= Comparative study

SR= Systemic Review study

NEONATAL OUTCOME

Infant born to HEV infected mother is highly potential and exposed to viral hepatitis E infection this is due to ability of the virus to undergo a cross infection either intrauterine, extra uterine or during lactation, six included studies report various chance of mother to infant HEV cross infection and chance of livelihood of the fetal, a study conducted at John Hopkins university USA in 2013 report [58]⁴⁴ live birth from hepatitis E infected pregnant mother were [32/55.1%] neonates tested HEV RNA both from cord blood and after 8-9 weeks of deliveries and out of these [32] neonates [11/34.3%] death was reported, another study conducted in India report [36]³² live birth were [15/41.6%] neonates tested anti HEV IgG positive out of these [4/26.6%] neonates reported die due to low birth weight and HEV infection related complication, a hospital based study meant to monitor HEV infected mother visiting hospital at Jammu & Kashmir conducted in 2019 reported [19]⁴ live birth in which of those [15/78.9%] infants tested positive of both serological and molecular method were [7/46.6] reported among the positive infants, another study performed in India report zero death [0] and [6] cross infection out of [93]³⁷ live birth delivered neonates this account for only [6.4%]³⁷ of infection among fetus born to HEV infected mother, this study also trace the chance of infection during breastfeeding found no any significant possibilities of infection this is due to insignificant viral loads titers in mother colostrum and high immune content of the colostrum milk that may inactivate or neutralize the virus to lost its infectivity³⁷. also [7] intrauterine death was reported in study conducted in India were [47] live birth also recorded in which of [9/19.1%] neonates was tested positive of anti HEV IgG and RNA but no death reported after delivery. Study with live birth of [128]³ conducted in India from 2011 to 2014 report [0] death among all born neonates while [59/46.0%] of neonates tested positive to anti HEV IgG were [15/25.4%] neonates cord was then tested HEV RNA positive.

FIG: B3. Show the characteristic of included study for neonatal outcomes

FIG: B3:

S/No	Study	Year	Sampling year	HEV infected pregnant women	Live birth	HEV Infected neonates	Neonates death	Country	REF
1	Rachana M chibber	2003	1994-1999	93	93	0	0	India	37
2	Yadav S	2016	2012-2014	50	36	7	4	India	32
3	Dr Ashok kumar	2017	2011-2014	144	128	59	0	India	31
4	Dr Gowri	2015	2010-2013	55	47	9	7	India	39
5	KRAIN	2014	2013	89	58	32	11	USA	44
6	MS KHUROO	2019	-----	26	19	15	7	INDIA	4

FIG: B3. CHARRACTERISTICS OF INCLUDED STUDY FOR NEONATES BORN TO HEV INFECTED MOTHER STUDY

Four included studies reported case fatality rate and mortality rate of both mothers and their neonates, a study from new Delhi India report a serious case fatality rate among neonates born to HEV infected mother, the study included 220 pregnant women were 132 test positive of anti HEV IgG and later 70/132 developed a fulminant hepatic failure, Of all 220 pregnant women 105 were deliver a live birth were mostly spontaneous vaginal deliveries only few undergo caesarean section. Out of [70] pregnant that developed fulminant hepatic failure and [116] pregnant non FHF delivered. Only 22/70 deliveries from fulminant hepatic failure has live births and 40/62 of non FHF, 30 neonatal death is reported and 20 maternal deaths, the study indicate significantly fewer live births were among HEV-infected women than non-HEV-infected women

A study conducted recently [2021] in Nigeria recruited 200 pregnant women were [56] tested positive of anti HEV IgG were 185/200 participants had a vaginal delivery, and 53/185 (28.65%) were seropositive to HEV antibodies, Four of the 200 (2.00%) participants had a spontaneous miscarriage with 2/4 (50.00%) being seropositive to HEV antibodies. were total of 9/200 (4.50%) reported stillbirth with 3/9 (33.33%) whom testing seropositive to HEV antibodies. maternal death 1/200(0.5%) was also reported in the study among pregnant tested positive to HEV antibodies (IgM) the study indicate maternal mortality among seropositive women as 1/58(1.72%)

A cross sectional study conducted among pregnant women reside in United Arab Emirates reported a very low death rate both in mother and their neonates the study included 469 pregnant women from different part of the Emirates were only 2/469 maternal death is recorded and 93/469 are seropositive to anti HEV IgG, 91/93 out infected pregnant women deliver a live birth were 26/91 neonates are tested positive and no any neonates was reported die throughout the study.

A study conducted in India at all India institute of medical sciences around 1997 to 1998 reported a high mortality rate among both pregnant women and their infants were 60 pregnant women are examine throughout the study 22/60 are tested seropositive and only 8/22 deliver live birth and 2/8 neonates tested positive of HEV RNA, 14 maternal were reported 13/14 before delivery and 1/14 just after delivery, Cord blood sample of the baby whose mother died Immediately after delivering the baby was tested positive for IgM anti-HEV as well as HEV RNA which is indication of intrauterine HEV infection⁴¹.

FIG: B4; show characteristics of included case fatality rate study.

FIG: B4

S/N O	Study	Year	Sampling yrs/country	Sample size	HEV Infected	Live birth	HEV Infected neonates	Maternal death	Neonates death	Study type	REF
1	Ike Innocent Mbachu	2021	---- INDIA	200	56	190	56	1	0	CS	40
2	Sarman Singh	2003	1997- 1998. INDIA	60	22	8	3	14		CS	41
3	RM Kumar	2001	2000. INDIA	469	93	91	26	2	0	CS	42
4	Sharda Patra	2007	2003- 2005. INDIA	220	132	105	----	20	30	HB	33

FIG: B4 CHARACTERISTIC OF INCLUDED DATA FOR CASE FATALITY RATE OF HEV INFECTED MOTHER AND THEIR FETUS

Abbreviation

HB= HOSPITAL BASE STUDY

CS= CROSS SECTIONAL STUDY

OBSERVATION

A seroprevalence of anti-HEV IgG antibody in pregnant women is totally differs by geographic location. HEV infection seroprevalence is seen high in most of the Indian study especially studies dated back in early 2000 and within 1990s but there is clear improvement in case reduction, case fatality rate both mortality rate in recent studies, the range of seroprevalence reported in study from India is 19% to 81.5%

HEV infection being endemic in African countries and other undeveloped region still most of report from Africa indicate an average low seroprevalence of HEV infection among pregnant women attending antenatal clinics and case fatality rate was recorded low among those infected with HEV during pregnancy

A decrease by years in case fatality rate and mortality rate among Indian pregnant women indicating some factors that may contributed in this current improvement of decline in HEV infection related death which may bring an attention of research of interest to analyze those factor and this would contribute in decreasing the number of infection and mortality from HEV infection in other region

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