

# Analysis of Causes of Hepatic Dysfunction in Obstetric Patients in India: A Systematic Review

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## ABSTRACT

**Background:** Epidemiology of liver disease in obstetric patients shows geographical variation depending upon the prevalence of preeclampsia, viral hepatitis, and tropical vector-borne diseases like malaria, leptospirosis, etc. We undertook the current systematic review to analyze the causes of hepatic dysfunction in obstetric patients in India and identify the gaps in the literature and reporting.

**Materials and methods:** We did a systematic review of studies reporting the causes of hepatic dysfunction in obstetric patients in India. A methodological quality assessment was done using a five-point questionnaire.

**Results:** A total of 21 studies qualified for evaluation. The rate of hepatic dysfunction among obstetric patients in India ranged from 0.15 to 3.3% with a mean and median rate of 1.49 and 0.93%, respectively. Preeclampsia/HELLP (mean = 36.0%, median = 31.4%, range: 3.6–83.8%) and viral hepatitis (mean = 34.1%, median = 35.5%, range: 5.1–61.8%) were the commonest causes of hepatic dysfunction. Other causes were intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy, tropical fever (malaria, leptospirosis, dengue, scrub typhus), etc. Maternal mortality ranged from 1.4 to 40% (mean = 12.6%, median = 10.0%) and perinatal mortality was between 16.4 and 38.70% (mean = 31.75%, median = 35.5%).

**Conclusion:** There is moderate quality evidence to show that preeclampsia/HELLP and viral hepatitis are the commonest causes of hepatic dysfunction in obstetric patients in India.

**Keywords:** Hepatic dysfunction, Obstetric patients, Preeclampsia, Viral hepatitis.

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## INTRODUCTION

Reducing maternal mortality across the globe is one of the priorities of sustainable development goals to be achieved by 2030.<sup>1</sup> According to the recent (2016–18) statistics reported by the Ministry of Health and Family Welfare, the maternal mortality ratio (MMR) of India is 113 per 100,000 live births. There is significant inequity within the country as states like Assam and Uttar Pradesh have an MMR of 215 and 197 per 100,000 live births, while states like Kerala and Maharashtra have an MMR as low as 43 and 46 per 100,000 live births, respectively.<sup>2</sup> With developing countries carrying a significant burden of maternal mortality, there is a need to focus on local epidemiology and develop protocolized care for obstetric patients based on regional guidelines.<sup>3</sup>

Among the various diseases causing maternal mortality and morbidity, liver disease can be challenging for clinicians. In 2019, a position statement was given by The Indian National Association for the Study of the Liver in collaboration with the Federation of Obstetric and Gynaecological Societies of India for the management of liver disease in pregnancy, but Indian epidemiological data have never been systematically reviewed in this field.<sup>4</sup>

Hepatic dysfunction in pregnancy can occur due to diverse etiologies and shows geographical variation. Broadly, it can be classified as liver diseases unique to pregnancy, liver diseases coincidental with pregnancy, and pregnancy in a patient with preexisting liver disease.<sup>5</sup> Indian epidemiology is unique due to the high prevalence of viral hepatitis and other tropical illnesses that can present with jaundice and encephalopathy syndrome, thus mimicking acute liver failure.<sup>6</sup> Differentiation of these causes is essential as diseases like malaria, leptospirosis, scrub typhus, etc., have specific treatment and are completely curable. Deepak

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and Patel studied acute liver failure in 28 patients admitted over a two-year period. Patients were classified as acute liver failure due to acute viral hepatitis (ALF-AVH) vs acute liver failure due to infectious disease (ALF-ID). Mortality was lower in ALF-ID (25%) patients as compared to ALF-AVH (50%). Causes of ALF-ID in the study group were typhoid fever, falciparum malaria, rickettsial infection, dengue fever, leptospirosis, amoebic liver abscess, and hemophagocytosis.<sup>7</sup>

Infectious causes of hepatic dysfunction also need to be differentiated from pregnancy-specific causes of hepatic dysfunction, as termination of pregnancy can help improve

maternal outcomes in some of the pregnancy-specific causes of hepatic dysfunction. Among the five pregnancy-specific diseases causing hepatic dysfunction, three (preeclampsia, HELLP, and acute fatty liver of pregnancy) are associated with more severe forms of liver disease and, together, termed as pregnancy-associated acute liver disease (PAALD). In a study including 87 pregnant patients with hepatic dysfunction, Devarbhavi et al. compared 46 PAALD patients with 41 patients of viral hepatitis. Mortality was 41 and 7.5% in the two groups, respectively. The authors reported the presence of ascites and hypertension as factors associated with a diagnosis of PAALD, triggering prompt delivery.<sup>8</sup>

Systematic reviews are a powerful tool to summarize available data in a particular field. The aim of the study was to analyze the causes of hepatic dysfunction in obstetric patients in the country. We undertook the current systematic review with the following objectives:

- To estimate the rate of hepatic dysfunction in obstetric patients in India
- To identify the causes of hepatic dysfunction in obstetric patients in India
- To identify the gaps in the literature and reporting of liver diseases in obstetric patients in India

## MATERIALS AND METHODS

### Study Selection

Studies reporting hepatic dysfunction and its causes in obstetric patients in India were considered eligible for analysis. An obstetric patient was defined as a pregnant woman or a woman within 42 days of delivery. Hepatic dysfunction was defined as clinical evidence of jaundice and/or total bilirubin of more than 2 mg/dL along with elevated liver enzymes above the physiological range. To generate more stable and reliable information, we excluded the studies with less than 25 patients. This cutoff was arbitrary. We further excluded those studies that did not include at least four of the following causes: viral hepatitis, preeclampsia/eclampsia, HELLP syndrome, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, tropical fever, hemolytic anemia, and chronic liver disease.

### Literature Search

A literature search was done in PubMed/Medline/Scopus/Google Scholar for original research articles using the terminology "Hepatic dysfunction in pregnancy," "Jaundice in pregnancy," "Liver disease

in pregnancy," "Hepatic dysfunction in obstetric patients," "Jaundice in obstetric patients," "Liver disease in obstetric patients." We included all case-control, cross-sectional, and cohort studies published in the English language between January 1, 2011, and December 31, 2020 (10 years). The bibliography of the relevant research articles was also searched for other suitable studies, and papers citing included studies were also reviewed. The title and abstract of documents found by the literature search were reviewed, and unsuitable manuscripts or duplicate results were excluded. The remaining papers were reviewed independently by two authors, and disagreements were resolved by consensus. Studies done in other geographical areas besides India were excluded. We also excluded the studies that only dealt with hepatitis in pregnancy (Flowchart 1).

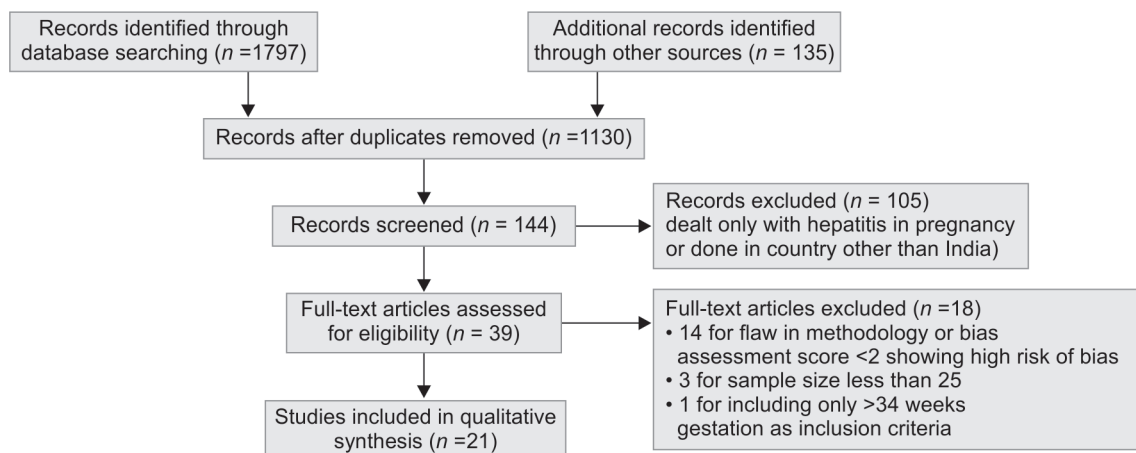
### Study Quality Assessment

A methodological quality assessment of the eligible studies was done to know the probability of bias in the information retrieved. Risk of bias assessment in epidemiological studies can be done using a standard assessment tool or by using a customized bias assessment tool developed specifically for the review. We chose the latter approach and developed our own questionnaire to assess the study quality after reviewing the literature for a bias assessment in epidemiological studies.<sup>9</sup> The studies were assessed with a 5-point questionnaire using the following attributes: (1) Reporting of well-defined appropriate patient recruitment criteria; (2) Use of robust approach to ascertain the cause of hepatic dysfunction; (3) Identification of all common causes of hepatic dysfunction in pregnancy to reduce the risk of misclassification of cause of hepatic dysfunction; (4) Sufficient number of patients having the cause of hepatic dysfunction ascertained (unclassified 10%); and (5) Reporting of the causes of maternal mortality in patients with hepatic dysfunction. Studies scoring two or more were included for analysis. A score of 5 was considered high-quality evidence, while a score of 3 or 4 was considered moderate-quality evidence. Scores less than 3 were considered poor quality evidence.

### Data Extraction

Data collection was done from the studies qualifying for analysis using a data extraction form. Information was retrieved from the full text of the studies under the following heading: the objective of the study, name of the first author, year, place, and duration of the study.

Flowchart 1: PRISMA flow diagram



Number and location of centers, study design, inclusion and exclusion criteria, rate of hepatic dysfunction, the total number of cases, maternal mortality, perinatal mortality, causes of hepatic dysfunction, and causes of maternal death were noted.

**Statistical Analysis**

We used Prism v 5.0 (Carlsbad, California, USA) and MedCalc Software for statistical analysis. Categorical variables were represented as frequencies and percentages. Causes of maternal mortality and hepatic dysfunction in pregnancy were represented as bar graphs.

**RESULTS**

Our search resulted in the identification of 1,797 records. After excluding the articles which did not qualify our study selection criteria, the full text of 39 articles was read for eligibility. Another 18 studies were excluded due to poor methodology, small sample size, or inclusion of only a subgroup of pregnant patients (see *Flowchart 1*). A total of 21 studies were included for the final analysis. The methodological quality assessment showed deficiencies in several areas of methodology. Sixteen studies were of moderate quality with a score of 3 (eight studies) or 4 (eight studies). Two studies had a score of 5, while three studies had a score of 2 (*Table 1*).<sup>10-30</sup>

**Study Characteristics**

Among the 21 studies included, five were conducted to study the clinical spectrum, causes, and outcome of hepatic dysfunction in pregnancy, while 16 were done to investigate the fetomaternal

outcome of jaundice during pregnancy. There were five retrospective studies and 16 prospective studies. All were single-center studies conducted in government hospitals except for five studies done in private hospitals. The duration of the study was from 6 to 30 months. The sample size ranged from 30 to 300 patients, with the largest sample from the government medical college of Bhopal (Madhya Pradesh). Maximum studies were from Mumbai, where three studies were conducted (*Fig. 1*). Most of the centers were in the northern and southern parts of the country. There are limited data from the eastern and central parts of the country. Fourteen studies included only admitted patients, whereas seven studies included both admitted as well as outpatients (*Table 2*).<sup>10-30</sup>

**Rate of Hepatic Dysfunction and Maternal Mortality**

Rate of hepatic dysfunction among pregnant women ranged from 0.15 to 3.3% with a mean and median rate of 1.49 and 0.93%. Similarly, maternal mortality ranged from 1.4 to 40% (mean = 12.6%, median = 10.0%) while perinatal mortality was between 16.4 and 38.70% (mean = 31.75%, median = 35.5%) (*Table 2*).<sup>10-30</sup>

**Causes of Hepatic Dysfunction during Pregnancy**

Preeclampsia and HELLP were the commonest causes of hepatic dysfunction (mean = 36.0%, median = 31.4%, range: 3.6-83.8%) followed by viral hepatitis (mean = 34.1%, median = 35.5%, range: 5.1-61.8%). Other causes included cholestasis of pregnancy (mean = 16.9%, median = 15.0%, range: 1.2-54.9%) followed by acute fatty liver of pregnancy (mean = 2.6%, median = 1.4%, range: 0-10.4%), tropical fever (mean = 2.5%, median = 0.8%, range:

**Table 1:** Bias assessment

Authors	Appropriate eligibility and recruitment of patients clearly defined	Confirmation of the cause of hepatic dysfunction with laboratory or autopsy	All common causes of hepatic dysfunction in pregnancy included	Unclassified causes of hepatic dysfunction 10%	Causes of maternal mortality given	Total score
Tiwari et al. <sup>10</sup>	X	X	O	O	O	3
Changede et al. <sup>11</sup>	X	X	O	O	O	3
Bhalla et al. <sup>12</sup>	O	X	O	O	O	4
Padh et al. <sup>13</sup>	X	O	O	O	X	3
Negi et al. <sup>14</sup>	O	O	O	O	O	5
Agarwal et al. <sup>15</sup>	O	X	O	O	O	4
Devi and Bhavani <sup>16</sup>	X	X	O	O	O	3
Choudhary et al. <sup>17</sup>	X	O	O	O	O	4
Kohli et al. <sup>18</sup>	X	O	O	O	O	4
Sunanda et al. <sup>19</sup>	O	X	O	O	O	4
Suresh et al. <sup>20</sup>	X	X	O	O	O	3
Tiwari et al. <sup>21</sup>	X	X	O	O	X	2
Solanke et al. <sup>22</sup>	X	O	O	O	O	4
Sharma et al. <sup>23</sup>	X	X	O	O	O	3
Mitta and Rao <sup>24</sup>	X	O	O	O	O	4
Krishnamoorthy and Murugesan <sup>25</sup>	X	X	O	O	O	3
Mishra et al. <sup>26</sup>	O	O	O	O	O	5
Satia and Jandhyala <sup>27</sup>	X	X	O	O	O	3
Dsouza et al. <sup>28</sup>	X	X	O	O	X	2
Singh et al. <sup>29</sup>	X	X	X	O	O	2
Nath et al. <sup>30</sup>	X	O	O	O	O	4

X, not answered; O, answered



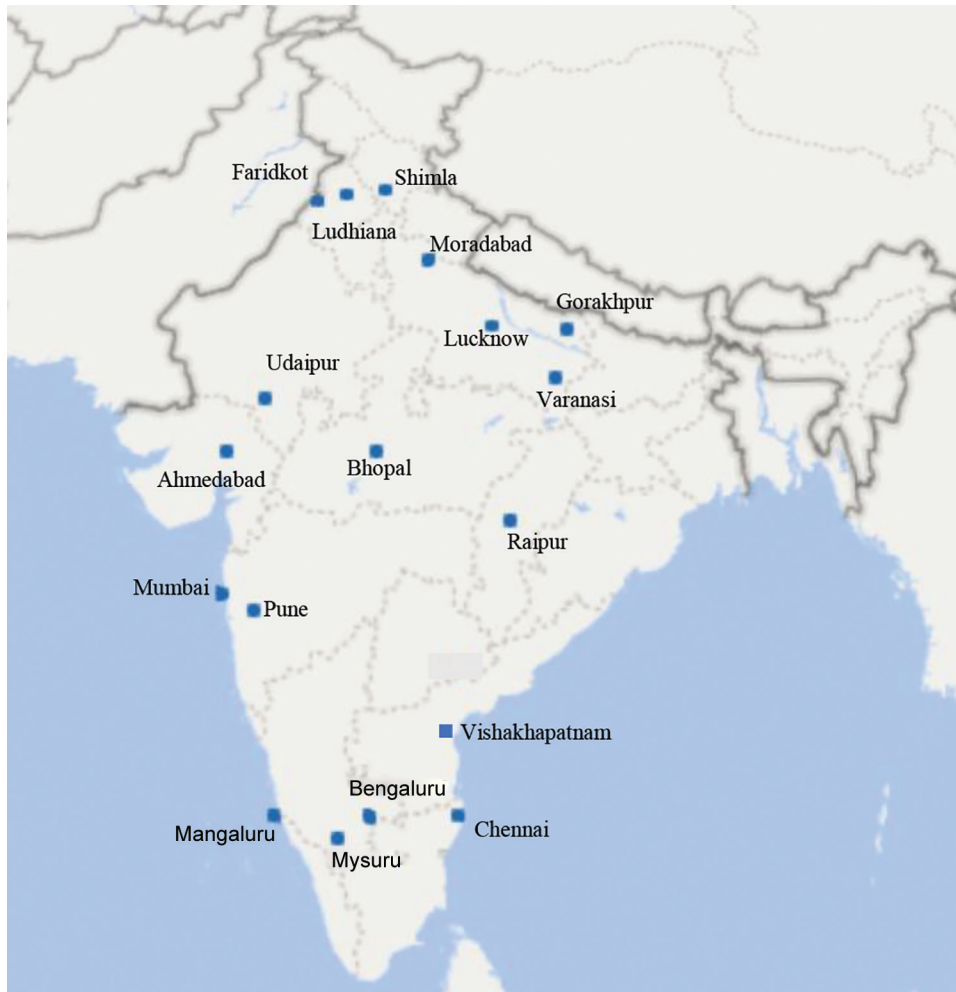


Fig. 1: Location of hospitals where studies were done

Table 2: Characteristics of studies included for the analysis of hepatic dysfunction in obstetric patients in the Indian subcontinent

Author	Study design	No of centers	Government/ private	Location	Study duration (years)	ANC/ PNC/ both	Outpatient/ admitted/ both	Rate (hepatic dysfunction) (%)	Maternal mortality (%)	Perinatal mortality (%)	Total cases
Tiwari et al. <sup>10</sup>	P	1	G	Bhopal	1	ANC	Admitted	NA	4.3	31	300
Changede et al. <sup>11</sup>	R	1	G	Mumbai	1	ANC	Admitted	NA	40	37	43
Bhalla et al. <sup>12</sup>	P	1	G	Faridkot	1	ANC	Both	3.1	5.9	NA	118
Padh et al. <sup>13</sup>	P	1	G	Ahmedabad	3.5	ANC	Admitted	0.32	12.85	35.71	70
Negi et al. <sup>14</sup>	P	1	G	Shimla	1	ANC	Both	3	7.14	NA	126
Agarwal et al. <sup>15</sup>	P	1	G	Lucknow	1	ANC	Admitted	1.2	39.3	37	122
Devi and Bhavani <sup>16</sup>	P	1	G	Vishakhapatnam	2	ANC	Admitted	0.72	12.74	35.71	102
Choudhary et al. <sup>17</sup>	P	1	G	Udaipur	1	ANC	Admitted	0.28	18.96	38	58
Kohli et al. <sup>18</sup>	R	1	G	Pune	2	ANC	Admitted	2.9	1.37	NA	146
Sunanda et al. <sup>19</sup>	P	1	G	Bengaluru	1.5	ANC	Both	0.15	13	25.8	31
Suresh et al. <sup>20</sup>	P	1	G	Mysore	2	ANC	Both	3.2	2.5	NA	197

(Contd...)

**Table 2:** (Contd...)

Author	Study design	No of centers	Government/ private	Location	Study duration (years)	ANC/ PNC/ both	Outpatient/ admitted/ both	Rate (hepatic dysfunction) (%)	Maternal mortality (%)	Perinatal mortality (%)	Total cases
Tiwari et al. <sup>21</sup>	P	1	G	Gorakhpur	1	ANC	Both	2.37	13	29.17	214
Solanki et al. <sup>22</sup>	P	1	G	Mumbai	2	ANC	Both	NA	24.2	38.7	103
Sharma et al. <sup>23</sup>	P	1	Pr	Bhopal	1	ANC	Admitted	NA	3.3	NA	30
Mitta and Rao <sup>24</sup>	P	1	Pr	Mangaluru	2	ANC	Admitted	0.31	4.76	30.76	42
Krishna moorthy and Murugesan <sup>25</sup>	P	1	G	Chennai	1	ANC	Admitted	0.29	7.8	35.5	51
Mishra et al. <sup>26</sup>	P	1	G	Raipur	1.5	ANC	Admitted	0.9	4	NA	80
Satia and Jandhyala <sup>27</sup>	R	1	G	Mumbai	1	both	Admitted	0.81	22	22	55
Dsouza et al. <sup>28</sup>	R	1	Pr	Ludhiana	1	ANC	Admitted	3.3	1.9	NA	51
Singh et al. <sup>29</sup>	R	1	G	Varanasi	0.5	ANC	Admitted	NA	15.3	NA	78
Nath et al. <sup>30</sup>	P	1	Pr	Moradabad	3	ANC	Both	0.95	10	16.4	100

R, retrospective; P, prospective; G, government hospital; Pr, private hospital; ANC, antenatal case; PNC, postnatal case; NA, not available

**Table 3:** Causes of hepatic dysfunction among obstetric patients in India

Authors	PE + HELLP	AFLP	Cholestasis	Viral hepatitis	Tropical fever	Hemolytic anemia	Undetected/ others	Total cases
Tiwari et al. <sup>10</sup>	69 (23%)	23 (7.7%)	14 (4.7%)	150 (50%)	0 (0.0%)	19 (6.3%)	25 (8.3%)	300
Changede et al. <sup>11</sup>	7 (16.3%)	1 (2.3%)	4 (9.3%)	21 (48.8%)	3 (7.0%)	3 (7.0%)	4 (9.3%)	43
Bhalla et al. <sup>12</sup>	73 (61.9%)	0 (0.0%)	16 (13.6%)	24 (20.3%)	0 (0.0%)	0 (0.0%)	5 (4.2%)	118
Padh et al. <sup>13</sup>	24 (34.3%)	0 (0.0%)	13 (18.5%)	27 (38.6%)	0 (0.0%)	2 (2.9%)	4 (5.7%)	70
Negi et al. <sup>14</sup>	33 (26.2%)	1 (0.8%)	42 (33.3%)	42 (33.3%)	1 (0.8%)	0 (0.0%)	7 (5.6%)	126
Agarwal et al. <sup>15</sup>	61 (50.0%)	11 (9.0%)	29 (23.8%)	21 (17.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	122
Devi and Bhavani <sup>16</sup>	32 (31.4%)	3 (2.9%)	4 (3.9%)	23 (22.5%)	12 (11.8%)	18 (17.6%)	10 (9.8%)	102
Choudhary et al. <sup>17</sup>	27 (46.6%)	6 (10.4%)	9 (15.5%)	11 (19.0%)	5 (8.6%)	0 (0.0%)	0 (0.0%)	58
Kohli et al. <sup>18</sup>	57 (39.0%)	2 (1.4%)	52 (35.6%)	33 (22.6%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	146
Sunanda et al. <sup>19</sup>	10 (32.3%)	1 (3.2%)	7 (22.6%)	11 (35.5%)	0 (0.0%)	0 (0.0%)	2 (6.4%)	31
Suresh et al. <sup>20</sup>	165 (83.7%)	0 (0.0%)	8 (4.1%)	10 (5.1%)	2 (1%)	0 (0.0%)	12 (6.1%)	197
Tiwari et al. <sup>21</sup>	142 (66.4%)	2 (0.9%)	36 (16.8%)	23 (10.7%)	0 (0.0%)	0 (0.0%)	11 (5.1%)	214
Solanki et al. <sup>22</sup>	25 (24.3%)	2 (1.9%)	8 (7.8%)	39 (37.8%)	5 (4.8%)	0 (0.0%)	24 (23.3%)	103
Sharma et al. <sup>23</sup>	14 (46.7%)	0 (0.0%)	2 (6.7%)	14 (46.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	30
Mitta and Rao <sup>24</sup>	9 (21.4%)	1 (2.4%)	6 (14.2%)	22 (52.4%)	2 (4.8%)	0 (0.0%)	2 (4.8%)	42
Krishnamoorthy and Murugesan <sup>25</sup>	7 (13.7%)	4 (7.8%)	3 (5.9%)	26 (51.0%)	2 (3.9%)	0 (0.0%)	9 (17.6%)	51
Mishra et al. <sup>26</sup>	65 (81.3%)	1 (1.2%)	1 (1.2%)	10 (12.5%)	1 (1.2%)	2 (2.5%)	0 (0.0%)	80
Satia and Jandhyala <sup>27</sup>	2 (3.6%)	0 (0.0%)	13 (23.6%)	34 (61.8%)	2 (3.6%)	0 (0.0%)	4 (7.2%)	55
Dsouza et al. <sup>28</sup>	11 (21.6%)	1 (2.0%)	28 (54.9%)	10 (19.6%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	51
Singh et al. <sup>29</sup>	10 (12.8%)	0 (0.0%)	20 (25.6%)	48 (61.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	78
Nath et al. <sup>30</sup>	20 (20.0%)	0 (0.0%)	15 (15.0%)	49 (49%)	5 (5.0%)	0 (0.0%)	11 (11.0%)	100

PE, pre-eclampsia; HELLP, haemolysis elevated liver enzymes and low platelets; AFLP, acute fatty liver of pregnancy

0–11.8%), and hemolytic anemia (mean = 1.7%, median = 0%, range: 0–17.7%). There were undetected/other causes like drug-induced liver dysfunction, hyperemesis gravidarum, malignancy, poisoning, and autoimmune hepatitis in around 5% of cases (mean = 6.1%, median = 5.6%, range: 0–23.3%).

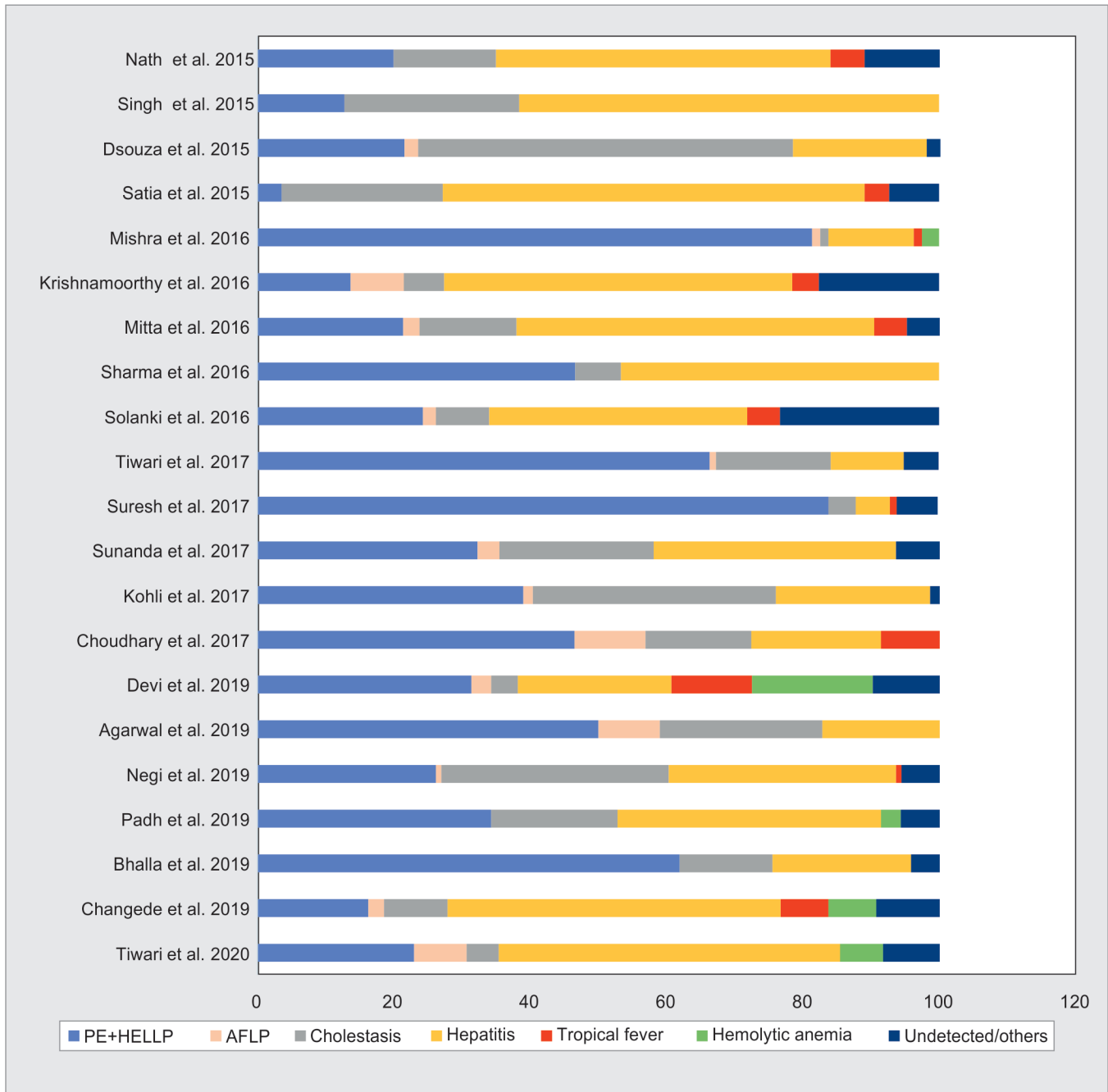
A similar trend was evident when study-wise causes were discussed. Almost all studies presented that preeclampsia,

HELLP, and viral hepatitis were the commonest causes of hepatic dysfunction during pregnancy (Table 3, Fig. 2).<sup>10–30</sup>

### Viral Hepatitis

Fifteen studies reported the causes of viral hepatitis. Overall, HEV was the commonest cause of viral hepatitis (mean = 41.1%, median = 45%, range: 4.5–85.7%) followed by HBV (mean = 34.9%; median = 33.3%,





**Fig. 2:** Causes of hepatic dysfunction in obstetric patients. PE, preeclampsia; HELLP, hemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy

range: 0–72%) and HAV (mean = 14.3%, median = 9.5%, range: 0–46.9%). HCV was reported as a cause of viral hepatitis in only six studies, all of which were from northern India (Lucknow, Varanasi, Moradabad, Faridkot, Ludhiana, and Bhopal) (Fig. 3).

**Tropical Fever**

Eleven studies reported the cause of tropical fever leading to hepatic dysfunction in pregnancy. Among the various reasons for tropical fever, malaria was the commonest followed by leptospirosis.

Two studies reported dengue hemorrhagic fever as the cause of hepatic dysfunction, one from Mumbai (one case) and another from Mysore (two cases).<sup>20,22</sup> Negi et al. reported one case of scrub typhus in his study, including 126 patients from Shimla.<sup>14</sup>

**Causes of Maternal Mortality**

Eighteen studies reported the cause of maternal mortality. Viral hepatitis and pregnancy-associated acute liver dysfunction due to preeclampsia, acute fatty liver of pregnancy, and HELLP syndrome were the commonest causes of mortality (Fig. 4). Agarwal et al. from Lucknow reported the maximum deaths due to hepatic encephalopathy, but arterial ammonia levels were not mentioned in the study.<sup>15</sup> There were no maternal deaths due to intrahepatic cholestasis of pregnancy or hyperemesis gravidarum.

No study reported autopsy findings. Immediate and antecedent causes of maternal mortality were not mentioned separately in any study.

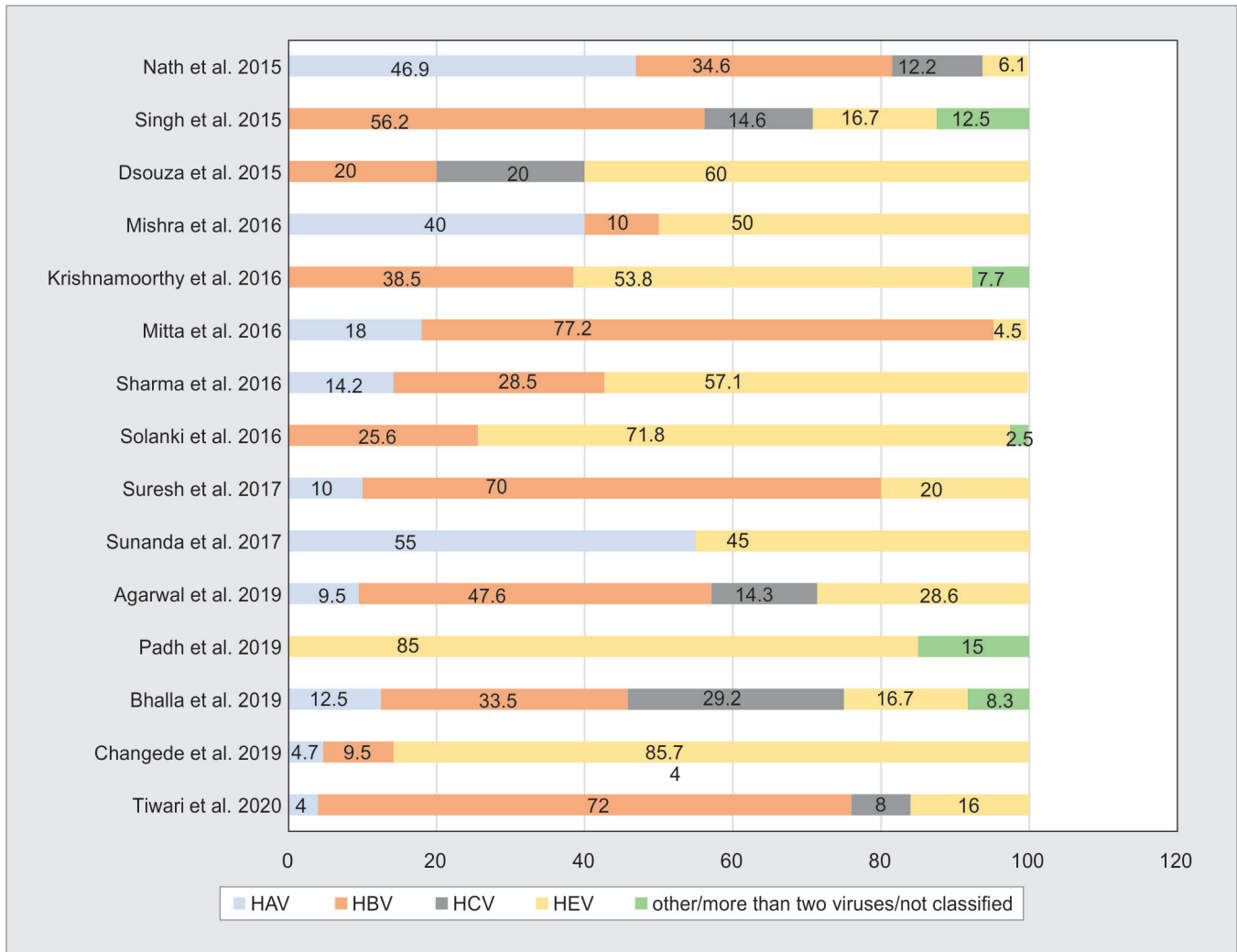


Fig. 3: Causes of hepatitis. HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus

## DISCUSSION

To the best of our knowledge, this is the first systematic review reporting causes of hepatic dysfunction in obstetric patients in India. Our systematic review showed that 70% of cases of hepatic dysfunction in obstetric patients are either due to preeclampsia/HELLP or viral hepatitis.

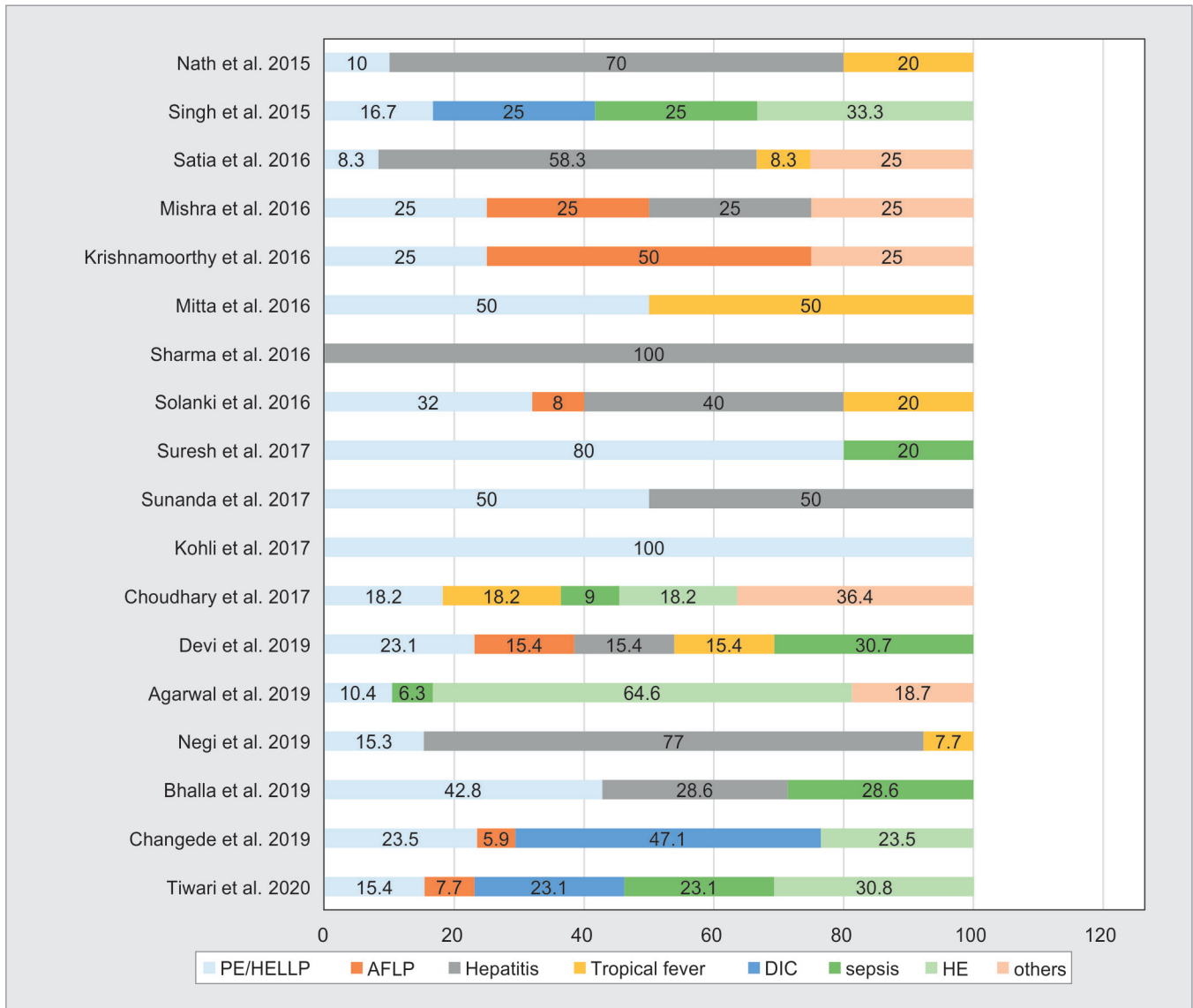
The rate of hepatic dysfunction in obstetric patients in India (0.15–3.3%) is comparable to other countries.<sup>31,32</sup>

Ch'ng et al. reported liver dysfunction in 3% of deliveries in a study from South Wales, United Kingdom.<sup>31</sup> A population-based study from the United States reported hepatic dysfunction due to causes unique to pregnancy in 0.77% of pregnant women. Of the five unique diseases of pregnancy that cause hepatic dysfunction, preeclampsia was the commonest (134 cases). It was followed by HELLP syndrome (72 cases), intrahepatic cholestasis of pregnancy (26 cases), hyperemesis gravidarum (14 cases), and acute fatty liver of pregnancy (1 case).<sup>32</sup> Diseases specific to pregnancy are the commonest causes of hepatic dysfunction in western countries, while viral hepatitis and tropical fever with jaundice are important differential diagnoses in developing countries like India. Variation

in the incidence of hepatic dysfunction within the country could be due to differences in inclusion criteria as some studies included outdoor and admitted patients while others included admitted patients only. Another reason for the difference in hepatic dysfunction incidence could be the difference in the prevalence of viral hepatitis in different geographical regions and study cohorts.

## Limitations

The current study has some limitations due to the lack of use of standardized definitions and surveillance guidelines. Hepatic dysfunction in pregnancy is an umbrella term. It includes antenatal cases and those who develop hepatic dysfunction in the postnatal period, but very few studies have included the latter subgroup (see Table 1). This leads to underreporting of hepatic dysfunction, especially due to postpartum preeclampsia, postpartum hemorrhage-induced shock liver, and sepsis-induced hepatic dysfunction. Although no study reported liver biopsy findings in any of the patients, 16 studies reported laboratory confirmation of the etiology of hepatic dysfunction. This is also because the primary objective of 16 studies was to study the fetomaternal outcome of hepatic dysfunction in pregnancy, while only five studies aimed at



**Fig. 4:** Causes of maternal mortality. PE, preeclampsia; HELLP, hemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy; DIC, disseminated intravascular coagulation; HE, hepatic encephalopathy

investigating the clinical profile, causes, and outcome of hepatic dysfunction in pregnancy.

Another limitation of our study is that we could not classify the causes of maternal mortality appropriately. None of the studies reported immediate, antecedent, and underlying causes of death separately.

It is evident from the current study that reporting of hepatic dysfunction in obstetric patients needs to be streamlined to generate robust data for protocolized care. We suggest using well-accepted standard definitions/diagnostic criteria for classifying the causes of hepatic dysfunction in pregnancy, e.g., Mississippi criteria for HELLP syndrome, Swansea criteria for acute fatty liver of pregnancy. We also suggest that postpartum patients should be included in the study cohort as sepsis and shock liver are significant differentials in this subgroup.

Besides this, maternal mortality reporting should be done in a standardized format for the correct understanding of the disease burden.

## CONCLUSION

Currently, moderate-quality evidence shows that hepatic dysfunction in pregnancy in India occurs due to several causes, of which viral hepatitis and preeclampsia/HELLP are the commonest. Mortality may vary depending upon the cause and duration of illness. Hospitals serving large populations from poor socioeconomic backgrounds show higher mortality as patients reach the hospital only late in the course of the disease. A structured national reporting format is needed to find the true epidemiology of hepatic dysfunction in obstetric patients in India. This will help better plan and direct funds in the right direction for ending preventable maternal mortality in one of the world's most populated countries.

## HIGHLIGHTS

- Hepatic dysfunction in obstetrics is associated with significant fetomaternal morbidity and mortality.



- It is important to differentiate between causes of hepatic dysfunction in obstetric patients as the treatment and outcome are different.
- There is a moderate quality of evidence to suggest that preeclampsia/HELLP and viral hepatitis are the major causes of hepatic dysfunction in obstetric patients in India.
- Among the various causes of viral hepatitis in obstetric patients in India, HEV hepatitis is the commonest followed by HBV hepatitis.
- There are considerable gaps in the reporting of causes of hepatic dysfunction in obstetric patients in India. A standardized national reporting format is needed to generate robust data and understand the true disease burden.

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