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# Dengue infections in India: A meta-analysis

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**Abstract:**

The escalating impact of dengue infection (DG-IF) on health and mortality is a critical issue, both nationally and globally. Therefore, it is of interest to assess the current trends of DG-IF in India. We meticulously searched through a wide range of internet databases to

gather comprehensive studies on the incidence, prevalence, sero-prevalence, cost effectiveness and mortality rate of DG-IF in India from 2014 to 2023 (10 years) in total of 127 studies. There was a significant heterogeneity in reported outcomes ( $p$ -values $<0.001$ ). Thus, public health strategies should include early detection of DG-IF in our country.

**Keywords:** Dengue, DENV, burden of dengue, seroprevalence, prevalence.

### Background:

A study has shown that DG-IF, which is caused by an arbovirus of the Genus *Flavivirus* and Family *Flaviviridae*, is one of the most prevalent, fast-spreading vector-borne diseases impacting people [1]. As a result, research has shown that DG disease may be clinically characterized as either mild DG, dengue with or without warning signals, or severe DG [1, 2]. According to a study, an estimated 105 million infections occur worldwide every year, only 51 million of which are symptomatic, making it a major public health issue [3]. Due to increasing worldwide travel and the geographical expansion of the *Aedes* vector mosquitoes, DENVs are transmitted on all major continents, with new cases occurring and spreading to formerly non-endemic locations [4]. The primary PM DG-IF is presumed to provide permanent sterilizing immunity against homologous serotypes; however, exceptions exist in human and animal experimental investigations [5, 6]. Secondary infection (SC) with an un-encountered serotype often leads to classical dengue fever (FV) and is linked to a heightened risk of severe sequelae [7, 8]. This is a significant risk factor for the heightened severity of DG-FV via the antibody-dependent enhancement (ADE) pathway [9]. A second DG-FV occurring within two years after the first IF is likely to be an asymptomatic infection, as shown by the neutralizing antibody titer [10]. Therefore, it is of interest to assess DG fever in India with the help of systematic review (SR) and meta-analysis (MA).

### Material and Method:

#### Protocol development:

In the present manuscript, written according to the PRISMA checklist, [11] only the scientific evidence of DG-IF current Trent in India was investigated. This SR protocol was a priori registered in The International Prospective Register of SR (Registration No: CRD42024552341).

#### Search strategy, Databases & Selection criteria:

We have searched in electronic databases such as Cochrane Library, Medline, Web of Science (WoS), PubMed, Scopus & Google Scholar for publications published between January 2014 and December 2023. **Appendix I: Search Strategy** contains all of the search strategy's details. We have specifically used date/year as a filter to search three databases i.e. (PubMed, Scopus/Elsevier, and Embase) from May 24-27, 2024. The Covidence application was used to screen abstracts.

#### Inclusion criteria:

- [1] All studies conducted in India on this topic regardless of their design, purpose, or population.
- [2] Incidence
- [3] Prevalence

- [4] Number of cases
- [5] Mortality
- [6] Burden
- [7] Complications
- [8] Virus serotype details/ seroprevalence

2 reviewers independently collected data from selected papers using a predefined data extraction form. Any discrepancies in it were resolved through consensus. The information that was extracted from studies includes year of publication, study setting, location, period, laboratory investigations, number of suspected patients tested & found positive, the age distribution of cases and details of dengue serotypes as shown in **table 1 to table 6 (Dataset I -VI)**

#### Data extraction & Review synthesis:

3 reviewers carried out the initial screening. The collected literature was first searched to remove duplicates before being entered into **Rayyan software** [132]. After that, the titles and abstracts were screened. In 2<sup>nd</sup> screening phase, 3 reviewers evaluated the selected papers based on their compliance with the eligibility standards. While the 2, independently shortlisted studies that met the design, participant, and result requirements. Disagreements were resolved by discussion and, if necessary, the involvement of a 3<sup>rd</sup> reviewer. Using a pre-designed data extraction form in Microsoft Excel, 3 reviewers independently gathered details from the selected research. Initially, the search results were imported into **Mendeley software** (Version 1.19.6) where duplicate records were removed.

#### The outcome measures were:

- [1] The prevalence of laboratory-confirmed dengue infection among clinically suspected patients in the research area, as reported in hospital/laboratory or community-based investigations during outbreaks.
- [2] Seroprevalence of dengue in the study population dengue fever conditions, dengue severity and Mortality rate among dengue patients those were confirmed in labs.
- [3] Primary & secondary infections present.
- [4] Cost of illness/burden which included reported direct and indirect costs associated with dengue hospitalization.
- [5] The non-structural protein-1 (NS1) antigen, immunoglobulin M (IgM) antibodies against DG virus, haem-agglutination inhibition (HI) antibodies against DG virus, RT-PCR positivity, or virus isolation was used to diagnose acute dengue infection in the clinically suspected patients. The measurement of IgG or neutralizing antibodies against the dengue virus was used to determine the seroprevalence of dengue.



Table 1: Dataset I-DG Proportion

| Sr. No. | Reference No. | Author                      | Year of Publication | Year of study       | Country | Study Type (Hospital/ Outbreak) | Case Definition Referred  | Number of patients tested (Total) | Number of people tested positive (Event) |
|---------|---------------|-----------------------------|---------------------|---------------------|---------|---------------------------------|---------------------------|-----------------------------------|--|
| 1       | 12            | Abhilash <i>et al.</i>      | 2016                | 2012-2013           | India   | Hospital                        | AFI                       | 1258                              | 386                                      |
| 2       | 13            | Afreen <i>et al.</i>        | 2015                | 2011-2014           | India   | Hospital                        | AFI                       | 604                               | 416                                      |
| 3       | 14            | Ahir <i>et al.</i>          | 2016                | 2014-2015           | India   | Hospital                        | Clinical Suspected Dengue | 1146                              | 148                                      |
| 4       | 15            | Ahmad <i>et al.</i>         | 2016                | 2012-2013           | India   | Hospital                        | AFI                       | 298                               | 93                                       |
| 5       | 16            | Ahmed <i>et al.</i>         | 2015                | 2010                | India   | Hospital                        | Clinical Suspected Dengue | 4370                              | 1700                                     |
| 6       | 17            | Amudhan <i>et al.</i>       | 2015                | 2010-2013           | India   | Hospital                        | Clinical Suspected Dengue | 4578                              | 1185                                     |
| 7       | 18            | Anand <i>et al.</i>         | 2016                | 2011                | India   | Hospital                        | WHO                       | 112                               | 94                                       |
| 8       | 19            | Arora <i>et al.</i>         | 2021                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 647                               | 170                                      |
| 9       | 20            | Badoni <i>et al.</i>        | 2023                | 2018-2019           | India   | Hospital                        | Clinical Suspected Dengue | 279                               | 222                                      |
| 10      | 21            | Barde <i>et al.</i>         | 2014                | 2011-2012           | India   | Hospital                        | NVBDCP                    | 138                               | 21                                       |
| 11      | 22            | Barde <i>et al.</i>         | 2015                | 2013                | India   | Outbreak                        | NVBDCP                    | 648                               | 321                                      |
| 12      | 23            | Barde <i>et al.</i>         | 2015                | 2012                | India   | Outbreak                        | WHO                       | 247                               | 115                                      |
| 13      | 24            | Barua <i>et al.</i>         | 2016                | 2014                | India   | Hospital                        | AFI                       | 156                               | 101                                      |
| 14      | 25            | Bhattacharya <i>et al.</i>  | 2017                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 218                               | 168                                      |
| 15      | 26            | Biswas <i>et al.</i>        | 2014                | 2012                | India   | Outbreak                        | Clinical Suspected Dengue | 100                               | 79                                       |
| 16      | 27            | Chakravarti <i>et al.</i>   | 2014                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 700                               | 280                                      |
| 17      | 28            | Changal <i>et al.</i>       | 2016                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 225                               | 114                                      |
| 18      | 29            | Deshkar <i>et al.</i>       | 2017                | 2012-2016           | India   | Hospital                        | Clinical Suspected Dengue | 15606                             | 3822                                     |
| 19      | 30            | Dhingra <i>et al.</i>       | 2020                | Feb 2014 - Oct 2015 | India   | Hospital                        | Clinical Suspected Dengue | 255                               | 216                                      |
| 20      | 31            | Dinkar <i>et al.</i>        | 2020                | 2012-2017           | India   | Hospital                        | Clinical Suspected Dengue | 900                               | 461                                      |
| 21      | 32            | Duthade <i>et al.</i>       | 2015                | 2014                | India   | Hospital                        | Clinical Suspected Dengue | 872                               | 233                                      |
| 22      | 33            | Gopal <i>et al.</i>         | 2016                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 50                                | 25                                       |
| 23      | 34            | Gopinath <i>et al.</i>      | 2023                | 2018-2022           | India   | Hospital                        | Clinical Suspected Dengue | 1383                              | 286                                      |
| 24      | 35            | Gusani <i>et al.</i>        | 2017                | 2014                | India   | Hospital                        | NVBDCP                    | 765                               | 331                                      |
| 25      | 36            | Henna <i>et al.</i>         | 2014                | 2010-2012           | India   | Hospital                        | Clinical Suspected Dengue | 7836                              | 2807                                     |
| 26      | 36            | Henna <i>et al.</i>         | 2014                | 2012-2013           | India   | Hospital                        | Clinical Suspected Dengue | 2228                              | 527                                      |
| 27      | 37            | Islam <i>et al.</i>         | 2016                | 2015                | India   | Hospital                        | AFI                       | 62                                | 18                                       |
| 28      | 38            | Jindal <i>et al.</i>        | 2014                | 2011                | India   | Hospital                        | Clinical Suspected Dengue | 1787                              | 586                                      |
| 29      | 39            | Joshua <i>et al.</i>        | 2016                | 2014-2015           | India   | Hospital                        | Clinical Suspected Dengue | 4952                              | 2442                                     |
| 30      | 40            | Kartick <i>et al.</i>       | 2017                | 2014                | India   | Outbreak                        | Clinical Suspected Dengue | 62                                | 27                                       |
| 31      | 41            | Kaup <i>et al.</i>          | 2014                | 2013-2014           | India   | Hospital                        | Clinical Suspected Dengue | 278                               | 62                                       |
| 32      | 42            | Khan <i>et al.</i>          | 2014                | 2012                | India   | Hospital                        | Clinical Suspected Dengue | 164                               | 107                                      |
| 33      | 43            | Lall <i>et al.</i>          | 2016                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 3163                              | 646                                      |
| 34      | 44            | Lata <i>et al.</i>          | 2017                | 2011                | India   | Hospital                        | Clinical Suspected Dengue | 812                               | 399                                      |
| 35      | 45            | Laul <i>et al.</i>          | 2016                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 192                               | 115                                      |
| 36      | 46            | Madan <i>et al.</i>         | 2018                | Jun-Aug 2016        | India   | Hospital                        | Clinical Suspected Dengue | 471                               | 102                                      |
| 37      | 47            | Mehta <i>et al.</i>         | 2014                | 2008-2011           | India   | Hospital                        | WHO                       | 903                               | 253                                      |
| 38      | 48            | Mishra <i>et al.</i>        | 2015                | 2009-2012           | India   | Hospital                        | Clinical Suspected Dengue | 433                               | 136                                      |
| 39      | 49            | Mistry <i>et al.</i>        | 2015                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 4366                              | 1802                                     |
| 40      | 50            | Mital <i>et al.</i>         | 2016                | 2015                | India   | Hospital                        | AFI                       | 90                                | 61                                       |
| 41      | 51            | Muruganandham <i>et al.</i> | 2014                | 2013                | India   | Outbreak                        | WHO                       | 23                                | 13                                       |
| 42      | 52            | Neeraja <i>et al.</i>       | 2014                | 2011-2013           | India   | Hospital                        | Clinical Suspected Dengue | 175                               | 109                                      |
| 43      | 53            | Nikam <i>et al.</i>         | 2015                | 2014                | India   | Hospital                        | Clinical Suspected Dengue | 1090                              | 300                                      |
| 44      | 54            | Nisarta <i>et al.</i>       | 2016                | 2015-2016           | India   | Hospital                        | Clinical Suspected Dengue | 90                                | 21                                       |
| 45      | 55            | Nujum <i>et al.</i>         | 2014                | 2011                | India   | Hospital                        | WHO                       | 851                               | 174                                      |
| 46      | 56            | Padhi <i>et al.</i>         | 2014                | 2010-2012           | India   | Hospital                        | WHO                       | 5102                              | 1074                                     |
| 47      | 57            | Padmapriya <i>et al.</i>    | 2017                | 2009-2014           | India   | Hospital                        | Clinical Suspected Dengue | 10099                             | 1927                                     |
| 48      | 58            | Palewar <i>et al.</i>       | 2023                | 2014-2020           | India   | Hospital                        | Clinical Suspected Dengue | 6495                              | 4689                                     |
| 49      | 59            | Patankar <i>et al.</i>      | 2014                | 2012                | India   | Hospital                        | Clinical Suspected Dengue | 4401                              | 927                                      |
| 50      | 60            | Patil <i>et al.</i>         | 2020                | Jan 2019 - Dec 2019 | India   | Hospital                        | WHO                       | 640                               | 220                                      |
| 51      | 61            | Pothapregada <i>et al.</i>  | 2016                | 2012-2015           | India   | Hospital                        | WHO                       | 398                               | 261                                      |
| 52      | 62            | Prakash <i>et al.</i>       | 2015                | 2011-2013           | India   | Hospital                        | Clinical Suspected Dengue | 4019                              | 886                                      |
| 53      | 63            | Prakash <i>et al.</i>       | 2023                | 2021                | India   | Hospital                        | Clinical Suspected Dengue | 250                               | 85                                       |
| 54      | 64            | Prudhivi <i>et al.</i>      | 2014                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 1180                              | 284                                      |
| 55      | 65            | Ramachandran <i>et al.</i>  | 2016                | 2010                | India   | Hospital                        | Clinical Suspected Dengue | 1666                              | 930                                      |
| 56      | 66            | Rao <i>et al.</i>           | 2016                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 1980                              | 745                                      |
| 57      | 67            | Saravanan <i>et al.</i>     | 2017                | 2012                | India   | Outbreak                        | NVBDCP                    | 600                               | 260                                      |
| 58      | 68            | Saswat <i>et al.</i>        | 2015                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 204                               | 73                                       |
| 59      | 69            | Savargaonka <i>et al.</i>   | 2018                | 2012-2015           | India   | Hospital                        | Clinical Suspected Dengue | 5536                              | 1536                                     |
| 60      | 70            | Shabnum <i>et al.</i>       | 2017                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 1054                              | 456                                      |
| 61      | 71            | Shah <i>et al.</i>          | 2019                | 2014-2016           | India   | Hospital                        | Clinical Suspected Dengue | 819                               | 125                                      |
| 62      | 72            | Shaikh <i>et al.</i>        | 2015                | 2010                | India   | Hospital                        | Clinical Suspected Dengue | 6554                              | 3202                                     |
| 63      | 73            | Sharma <i>et al.</i>        | 2016                | 2015                | India   | Hospital                        | WHO                       | 60                                | 16                                       |
| 64      | 74            | Sharma <i>et al.</i>        | 2014                | 2013                | India   | Hospital                        | Clinical Suspected Dengue | 659                               | 141                                      |
| 65      | 75            | Shobha <i>et al.</i>        | 2014                | 2013                | India   | Outbreak                        | WHO                       | 68                                | 13                                       |
| 66      | 76            | Siddiqui <i>et al.</i>      | 2016                | 2015                | India   | Hospital                        | Clinical Suspected Dengue | 7177                              | 2358                                     |
| 67      | 77            | Singh <i>et al.</i>         | 2014                | 2013                | India   | Hospital                        | AFI                       | 1141                              | 812                                      |
| 68      | 78            | Singh <i>et al.</i>         | 2016                | 2015-2016           | India   | Hospital                        | Clinical Suspected Dengue | 2709                              | 1538                                     |
| 69      | 79            | Singh <i>et al.</i>         | 2016                | 2015                | India   | Hospital                        | WHO                       | 1100                              | 400                                      |
| 70      | 80            | Singh <i>et al.</i>         | 2023                | 2022                | India   | Outbreak                        | WHO                       | 63280                             | 2060                                     |
| 71      | 81            | Singla <i>et al.</i>        | 2015                | 2011-2012           | India   | Hospital                        | AFI                       | 300                               | 22                                       |

|    |    |                                |      |                     |       |          |                           |     |     |
|----|----|--------------------------------|------|---------------------|-------|----------|---------------------------|-----|-----|
| 72 | 82 | Somasundaram <i>et al.</i>     | 2019 | Jun 2017 - Nov 2017 | India | Hospital | Clinical Suspected Dengue | 325 | 232 |
| 73 | 83 | Sushi <i>et al.</i>            | 2014 | 2011                | India | Hospital | AFI                       | 100 | 8   |
| 74 | 84 | Tazeen <i>et al.</i>           | 2017 | 2014                | India | Hospital | Clinical Suspected Dengue | 60  | 48  |
| 75 | 85 | Vakrani <i>et al.</i>          | 2017 | 2013-2015           | India | Hospital | WHO                       | 139 | 101 |
| 76 | 86 | Venkatasubramani <i>et al.</i> | 2015 | 2010-2012           | India | Hospital | Clinical Suspected Dengue | 331 | 49  |
| 77 | 87 | Verma <i>et al.</i>            | 2016 | 2016                | India | Hospital | Clinical Suspected Dengue | 254 | 65  |
| 78 | 88 | Yogeesha <i>et al.</i>         | 2014 | 2012                | India | Hospital | Clinical Suspected Dengue | 200 | 80  |

Table 2: Data set II-DG Age Distribution

| Sr. No. | Ref. No. | Author                  | Year of publication | Year of study        | Study. Type | Avg./Median Age |
|---------|----------|-------------------------|---------------------|----------------------|-------------|-----------------|
| 1       | 16       | Ahmed <i>et al.</i>     | 2015                | 2010                 | Hospital    | 25              |
| 2       | 89       | Athira <i>et al.</i>    | 2018                | 2015-2017            | Hospital    | 7.6             |
| 3       | 22       | Barde <i>et al.</i>     | 2015                | 2012                 | Outbreak    | 33              |
| 4       | 23       | Barde <i>et al.</i>     | 2015                | 2013                 | Outbreak    | 35              |
| 5       | 29       | Deshkar <i>et al.</i>   | 2017                | 2012-2016            | Hospital    | 14              |
| 6       | 32       | Duthade <i>et al.</i>   | 2015                | 2014                 | Hospital    | 19              |
| 7       | 35       | Gusani <i>et al.</i>    | 2017                | 2014                 | Hospital    | 24              |
| 8       | 90       | Jain <i>et al.</i>      | 2017                | Aug-Nov 2015         | Hospital    | 30.9            |
| 9       | 91       | John <i>et al.</i>      | 2019                | 2014-2018            | Hospital    | 31.3            |
| 10      | 41       | Kaup <i>et al.</i>      | 2014                | 2013-2014            | Hospital    | 26              |
| 11      | 92       | Kumar <i>et al.</i>     | 2018                | Jan 2013 - June 2014 | Hospital    | 7.8             |
| 12      | 44       | Lata <i>et al.</i>      | 2012                | 2011                 | Hospital    | 36              |
| 13      | 48       | Mishra <i>et al.</i>    | 2015                | 2009-2012            | Hospital    | 7               |
| 14      | 93       | Mishra <i>et al.</i>    | 2018                | 2017                 | Hospital    | 33              |
| 15      | 49       | Mistry <i>et al.</i>    | 2015                | 2013                 | Hospital    | 22              |
| 16      | 56       | Padhi <i>et al.</i>     | 2014                | 2010-2012            | Hospital    | 23              |
| 17      | 58       | Palewar <i>et al.</i>   | 2023                | 2014-2020            | Hospital    | 25              |
| 18      | 59       | Patankar <i>et al.</i>  | 2014                | 2012                 | Hospital    | 23              |
| 19      | 60       | Patil <i>et al.</i>     | 2020                | Jan 2019 - Dec 2019  | Hospital    | 35.3            |
| 20      | 94       | Pereira <i>et al.</i>   | 2018                | Not Mentioned        | Hospital    | 32.41           |
| 21      | 64       | Prudhivi <i>et al.</i>  | 2014                | 2013                 | Hospital    | 32              |
| 22      | 66       | Rao <i>et al.</i>       | 2016                | 2013                 | Hospital    | 17              |
| 23      | 95       | Ravikumar <i>et al.</i> | 2021                | Aug-Dec 2020         | Hospital    | 8               |
| 24      | 67       | Saravanan <i>et al.</i> | 2016                | 2012                 | Outbreak    | 33              |
| 25      | 70       | Shabnum <i>et al.</i>   | 2017                | 2015                 | Hospital    | 26              |
| 26      | 96       | Sharma <i>et al.</i>    | 2014                | 2013                 | Hospital    | 16              |
| 27      | 83       | Sushi <i>et al.</i>     | 2014                | 2011                 | Hospital    | 21              |
| 28      | 97       | Swain <i>et al.</i>     | 2019                | 2010-2016            | Hospital    | 31.6            |
| 29      | 88       | Yogeesha <i>et al.</i>  | 2014                | 2012                 | Hospital    | 35              |
| 30      | 98       | Esther <i>et al.</i>    | 2023                | 2012-2017            | Hospital    | 32              |

Table 3: Dataset III-DG Fever (FV) and DG Severity (SV)

| Sr. No. | Ref. No. | Author                     | Year of Publication | Year of study              | WHO Case Definition Reference | Dengue Positives | DF   | Severe |
|---------|----------|----------------------------|---------------------|----------------------------|-------------------------------|------------------|------|--------|
| 1       | 12       | Abhilash <i>et al.</i>     | 2016                | 2012-2013                  | WHO 1997                      | 386              | 329  | 57     |
| 2       | 16       | Ahmed <i>et al.</i>        | 2015                | 2010                       | WHO 1997                      | 1700             | 1525 | 175    |
| 3       | 19       | Arora <i>et al.</i>        | 2021                | 2015                       | WHO 2009                      | 170              | 106  | 34     |
| 4       | 89       | Athira <i>et al.</i>       | 2018                | 2015-2017                  | WHO 2009                      | 34               | 31   | 11     |
| 5       | 28       | Changal <i>et al.</i>      | 2016                | 2015                       | WHO 1997                      | 114              | 84   | 30     |
| 6       | 99       | Chatterjee <i>et al.</i>   | 2014                | 2012                       | WHO 1997                      | 180              | 128  | 52     |
| 7       | 100      | Chhotala <i>et al.</i>     | 2016                | 2014-2015                  | WHO 1997                      | 100              | 94   | 6      |
| 8       | 101      | Deme <i>et al.</i>         | 2021                | August 2018 - October 2019 | WHO 2012                      | 200              | 200  | 116    |
| 9       | 29       | Deshkar <i>et al.</i>      | 2017                | 2012-2016                  | WHO 1997                      | 3822             | 3341 | 481    |
| 10      | 102      | Deshmukh <i>et al.</i>     | 2014                | 2012-2014                  | WHO 1997                      | 247              | 173  | 74     |
| 11      | 30       | Dhingra <i>et al.</i>      | 2020                | Feb 2014 - Oct 2015        | WHO 2013                      | 216              | 94   | 33     |
| 12      | 91       | John <i>et al.</i>         | 2019                | April 2014 - October 2018  | WHO 2012                      | 369              | 198  | 171    |
| 13      | 103      | Kumar <i>et al.</i>        | 2017                | 2015-2016                  | WHO 1997                      | 159              |      | 69     |
| 14      | 92       | Kumar <i>et al.</i>        | 2018                | Jan 2013 - June 2014       | WHO 2012                      | 40               | 20   | 20     |
| 15      | 45       | Laul <i>et al.</i>         | 2016                | 2015                       | WHO 1997                      | 306              | 119  | 56     |
| 16      | 104      | Meena <i>et al.</i>        | 2016                | 2014                       | WHO 1997                      | 115              | 89   | 26     |
| 17      | 105      | Mishra <i>et al.</i>       | 2016                | 2013-2015                  | WHO 2007                      | 100              | 84   | 16     |
| 18      | 106      | Misra <i>et al.</i>        | 2015                | 2003-2014                  | WHO 1997                      | 97               | 84   | 13     |
| 19      | 56       | Padhi <i>et al.</i>        | 2014                | 2010-2012                  | WHO 1997                      | 116              | 82   | 34     |
| 20      | 94       | Pereira <i>et al.</i>      | 2018                | Not Mentioned              | WHO 2009                      | 1074             | 1048 | 26     |
| 21      | 107      | Pothapregada <i>et al.</i> | 2015                | 2012 - 2014                | WHO 2007                      | 550              | 547  | 101    |
| 22      | 108      | Rathod <i>et al.</i>       | 2018                | 2013-2015                  | WHO 2009                      | 254              | 159  | 95     |
| 23      | 95       | Ravikumar <i>et al.</i>    | 2021                | Aug-Dec 2020               | WHO 2009                      | 100              | 100  | 11     |
| 24      | 109      | Sahana <i>et al.</i>       | 2015                | 2012-2013                  | WHO 2007                      | 44               | 43   | 30     |
| 25      | 74       | Sharma <i>et al.</i>       | 2016                | 2015                       | WHO 1997                      | 81               | 61   | 20     |
| 26      | 110      | Sil <i>et al.</i>          | 2016                | 2015-2016                  | WHO 1997                      | 16               | 5    | 11     |
| 27      | 79       | Singh <i>et al.</i>        | 2016                | 2015                       | WHO 1997                      | 71               | 62   | 9      |
| 28      | 111      | Singh <i>et al.</i>        | 2022                | Sept-Dec 2019              | WHO 1997                      | 400              | 260  | 140    |
| 29      | 82       | Somasundaram <i>et al.</i> | 2019                | Jun 2017 - Nov 2017        | WHO 2012                      | 1349             | 459  | 34     |
| 30      | 112      | Srividhya <i>et al.</i>    | 2017                | 2013                       | WHO 1997                      | 232              | 232  | 38     |
| 31      | 85       | Vakrani <i>et al.</i>      | 2017                | 2013-2015                  | WHO 1997                      | 140              | 70   | 70     |

Table 4: Dataset IV

| Sr. No. | Ref. No. | Author                       | Year of Publication | Study Year          | Total Positive for Dengue | No. of Mortality |
|---------|----------|------------------------------|---------------------|---------------------|---------------------------|------------------|
| 1       | 12       | Abhilash <i>et al.</i>       | 2016                | 2012-2013           | 386                       | 9                |
| 2       | 113      | Acharya <i>et al.</i>        | 2018                | 2017-2018           | 364                       | 14               |
| 3       | 15       | Ahmad <i>et al.</i>          | 2016                | 2012-2013           | 93                        | 4                |
| 4       | 16       | Ahmed <i>et al.</i>          | 2015                | 2010                | 1700                      | 1                |
| 5       | 21       | Barde <i>et al.</i>          | 2014                | 2011-2012           | 21                        | 0                |
| 6       | 22       | Barde <i>et al.</i>          | 2015                | 2012                | 321                       | 5                |
| 7       | 24       | Barua <i>et al.</i>          | 2016                | 2014                | 101                       | 1                |
| 8       | 114      | Bhalla <i>et al.</i>         | 2014                | 2011                | 299                       | 2                |
| 9       | 25       | Bhattacharya <i>et al.</i>   | 2017                | 2013                | 168                       | 0                |
| 10      | 99       | Chatterjee <i>et al.</i>     | 2014                | 2012                | 180                       | 7                |
| 11      | 100      | Chhotala <i>et al.</i>       | 2016                | 2014-2015           | 100                       | 4                |
| 12      | 29       | Deshkar <i>et al.</i>        | 2017                | 2012-2016           | 3822                      | 40               |
| 13      | 102      | Deshmukh <i>et al.</i>       | 2014                | 2012-2014           | 247                       | 11               |
| 14      | 115      | Deshwal <i>et al.</i>        | 2015                | 2013                | 515                       | 4                |
| 15      | 30       | Dhingra <i>et al.</i>        | 2020                | Feb 2014 - Oct 2015 | 216                       | 13               |
| 16      | 32       | Duthade <i>et al.</i>        | 2015                | 2014                | 233                       | 5                |
| 18      | 90       | Jain <i>et al.</i>           | 2017                | 2015                | 369                       | 19               |
| 19      | 116      | Krishnamoorthy <i>et al.</i> | 2017                | 2013                | 1308                      | 23               |
| 20      | 44       | Lata <i>et al.</i>           | 2012                | 2011                | 399                       | 0                |
| 21      | 105      | Mishra <i>et al.</i>         | 2016                | 2013-2015           | 97                        | 1                |
| 22      | 117      | Nagaram <i>et al.</i>        | 2017                | 2015-2016           | 174                       | 9                |
| 23      | 52       | Neeraja <i>et al.</i>        | 2014                | 2011-2013           | 109                       | 9                |
| 24      | 83       | Nimmagadda <i>et al.</i>     | 2014                | 2010 - 2012         | 150                       | 3                |
| 25      | 118      | Nimonkar R                   | 2022                | 2016                | 145                       | 1                |
| 26      | 118      | Nimonkar R                   | 2022                | 2017                | 107                       | 0                |
| 27      | 118      | Nimonkar R                   | 2022                | 2018                | 93                        | 1                |
| 28      | 118      | Nimonkar R                   | 2022                | 2019                | 242                       | 2                |
| 29      | 118      | Nimonkar R                   | 2022                | 2020                | 20                        | 0                |
| 30      | 119      | Padyana <i>et al.</i>        | 2019                | 2015                | 1170                      | 20               |
| 31      | 120      | Pai Jakribettu <i>et al.</i> | 2015                | 2013-2014           | 60                        | 2                |
| 32      | 107      | Pothapregada <i>et al.</i>   | 2015                | 2012 - 2014         | 254                       | 6                |
| 33      | 107      | Pothapregada <i>et al.</i>   | 2015                | 2012-2014           | 261                       | 6                |
| 34      | 63       | Prakash P                    | 2023                | 2021                | 85                        | 2                |
| 35      | 66       | Rao <i>et al.</i>            | 2016                | 2013                | 745                       | 0                |
| 36      | 109      | Sahana <i>et al.</i>         | 2015                | 2012-2013           | 81                        | 2                |
| 37      | 121      | Sahu <i>et al.</i>           | 2014                | 2011-2013           | 486                       | 5                |
| 38      | 67       | Saravanan <i>et al.</i>      | 2016                | 2012                | 260                       | 7                |
| 39      | 122      | Saroj <i>et al.</i>          | 2017                | 2015                | 172                       | 16               |
| 40      | 73       | Sharma <i>et al.</i>         | 2016                | 2015-2016           | 200                       | 0                |
| 41      | 74       | Sharma <i>et al.</i>         | 2016                | 2015-2016           | 107                       | 0                |
| 42      | 96       | Sharma <i>et al.</i>         | 2014                | 2013                | 141                       | 0                |
| 43      | 77       | Singh <i>et al.</i>          | 2014                | 2013                | 812                       | 12               |
| 44      | 80       | Singh <i>et al.</i>          | 2022                | Sept-Dec 2019       | 1349                      | 6                |
| 45      | 123      | Singhal <i>et al.</i>        | 2020                | 2017                | 575                       | 15               |
| 46      | 112      | Srividya <i>et al.</i>       | 2017                | 2013                | 140                       | 1                |
| 47      | 85       | Vakrani <i>et al.</i>        | 2017                | 2013-2015           | 101                       | 0                |
| 48      | 87       | Verma <i>et al.</i>          | 2014                | 2013                | 60                        | 4                |

Table 5: Dataset V

| Sr. No. | Ref. No. | Author                   | Year of Publication | Year of study | Total Tested | Primary (PM) | Secondary (SC) |
|---------|----------|--------------------------|---------------------|---------------|--------------|--------------|----------------|
| 1       | 22       | Barde <i>et al.</i>      | 2015                | 2012          | 115          | 111          | 4              |
| 2       | 28       | Changal <i>et al.</i>    | 2016                | 2015          | 114          | 38           | 76             |
| 3       | 33       | Gopal <i>et al.</i>      | 2016                | 2013          | 25           | 13           | 12             |
| 4       | 41       | Kaup <i>et al.</i>       | 2014                | 2013-2014     | 62           | 52           | 10             |
| 5       | 42       | Khan <i>et al.</i>       | 2014                | 2012          | 87           | 82           | 5              |
| 6       | 105      | Mishra <i>et al.</i>     | 2016                | 2013-2015     | 94           | 83           | 11             |
| 8       | 52       | Neeraja <i>et al.</i>    | 2014                | 2011-2013     | 109          | 87           | 22             |
| 9       | 53       | Nikam <i>et al.</i>      | 2015                | 2014          | 300          | 224          | 76             |
| 10      | 57       | Padmapriya <i>et al.</i> | 2017                | 2009-2014     | 1752         | 1124         | 628            |
| 11      | 66       | Rao <i>et al.</i>        | 2016                | 2013          | 22           | 21           | 1              |
| 12      | 124      | Rashmi <i>et al.</i>     | 2015                | 2014          | 97           | 93           | 4              |
| 13      | 115      | Shabnum <i>et al.</i>    | 2017                | 2015          | 456          | 442          | 14             |
| 14      | 76       | Siddiqui <i>et al.</i>   | 2016                | 2015          | 76           | 24           | 52             |
| 15      | 85       | Vikram <i>et al.</i>     | 2016                | 2013          | 22           | 8            | 14             |

Table 6: Dataset VI

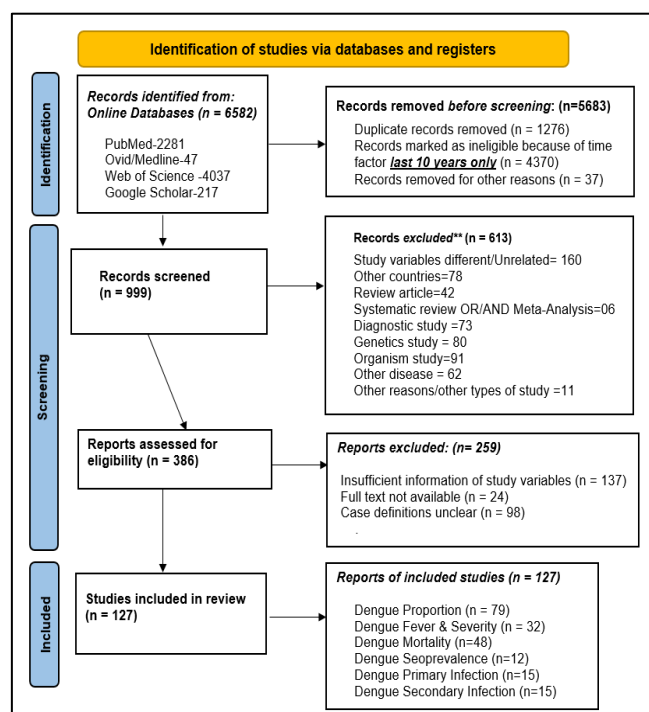
| Sr. No. | Ref. No. | Author                  | Publication Year | Study Year | Total Tested | Tested as Seropositive |
|---------|----------|-------------------------|------------------|------------|--------------|------------------------|
| 1       | 126      | Alagarasu <i>et al.</i> | 2023             | 2009-2019  | 2451         | 1963                   |
| 2       | 20       | Badoni <i>et al.</i>    | 2023             | 2018-2019  | 279          | 143                    |
| 3       | 127      | Garg <i>et al.</i>      | 2017             | 2011-2012  | 2558         | 1525                   |
| 4       | 128      | Lakshmi <i>et al.</i>   | 2022             | 2016-2019  | 5147         | 1314                   |
| 5       | 125      | Mishra <i>et al.</i>    | 2018             | 2017       | 1434         | 1163                   |



|    |     |                                   |      |                     |       |      |
|----|-----|-----------------------------------|------|---------------------|-------|------|
| 6  | 129 | Murhekar <i>et al.</i>            | 2019 | 2017-2018           | 12300 | 5338 |
| 7  | 130 | Oruganti <i>et al.</i>            | 2014 | Not mentioned       | 200   | 179  |
| 8  | 60  | Patil <i>et al.</i>               | 2020 | Jan 2019 - Dec 2020 | 640   | 398  |
| 9  | 131 | Rodríguez-Barraquer <i>et al.</i> | 2015 | 2011                | 800   | 744  |
| 10 | 132 | Vikram <i>et al.</i>              | 2016 | 2013                | 1899  | 542  |

## Results:

Initially, we searched 6582 published articles in various electronic databases such as PubMed-2281, Ovid/Medline-47, Web of Science -4037 and Google Scholar-217 published. This was later on narrowed down to 999 unique articles after duplicate removal over the last 10 years. Following titles and abstracts screening, 613 articles were excluded, leaving 386 articles for full-text evaluation. This resulted in 127 studies being selected for analysis [17-140] as shown in **Figure 1**.



**Figure 1:** PRISMA flowchart for inclusion

## Prevalence/proportion of laboratory dg cases & outbreak:

The clinically suspected patients are provided by 78 out of the 127 published studies included in this synthesis. This comprised 8 studies reporting outbreak investigations and 71 studies conducted in hospital or laboratory settings. A proportion of the studies that the hospital validated were conducted at the time; that the affected areas were going through an outbreak. The data of laboratory-confirmed cases by month were supplied by 32 research (40.5%) out of the 79 studies that reported a PP of DG cases; the majority of these studies (n = 53, 67%) indicated increased DG positivity throughout the rainy seasons, particularly from July to October. The majority of the forty-seven investigations identified acute dengue infection using a single test, as follows: detection of the NS1 antigen = 1, virus isolation = 1, RT-PCR = 7, HI antibodies = 2 and IgM antibodies = 36. The other studies employed multiple tests.

## Case definitions used:

While discussed about case studies their; we took assistance of WHO (World Health Organizations), NVBDCP (National Center for Vector Borne Diseases Control) & AFI (Acute Febrile Illness) case definitions. Out of 79 studies during hospital settings majority n=53 were clinical suspected dengue followed by n=13 WHO case definition, n=9 AFI case definition and the remaining studies n=4 were used NVBDCP case definitions respectively. Both hospital confirmed dengue study and showed similarly, among 71 hospital confirmed dengue cases n=51 were clinical suspected dengue followed by n=9 WHO case definition, n=9 AFI case definition and the remaining studies n=2 were used NVBDCP case definitions respectively. Among the reported outbreaks, investigators used n=4 WHO case definition, n=2 AFI case definition and the remaining studies n=2 were used NVBDCP case definitions respectively.

## Dengue proportion in India:

Based on testing of 206783 clinically suspected individuals from 78 studies, the overall estimate of the prevalence of laboratory-confirmed dengue infection in the random effects model was 39.4% (95% CI: 35.6%-44.67%) as shown in **Figure 2**. The heterogeneity was assessed by Hedge g statistics. The heterogeneity (HTG) overcomes by using REM as shown in **Figure 3**. The publication biased(PB) was assessed by using funnel plot, some asymmetry observed because individual study had different proportion and this was directly impacts on shifting the points on funnel to outside but the both the side almost normality hence in our study there was no PB was reporting as shown in. The prevalence reported by the 79 studies showed significant HTG (LRT p<0.001). In comparison to hospital-based surveillance (HBS) studies (40%, 95% CI: 35-44), the prevalence of laboratory-confirmed DG-IF was nearly identical in studies reporting outbreaks (OB) or HBS studies during OB (39%, 95% CI: 34-44).

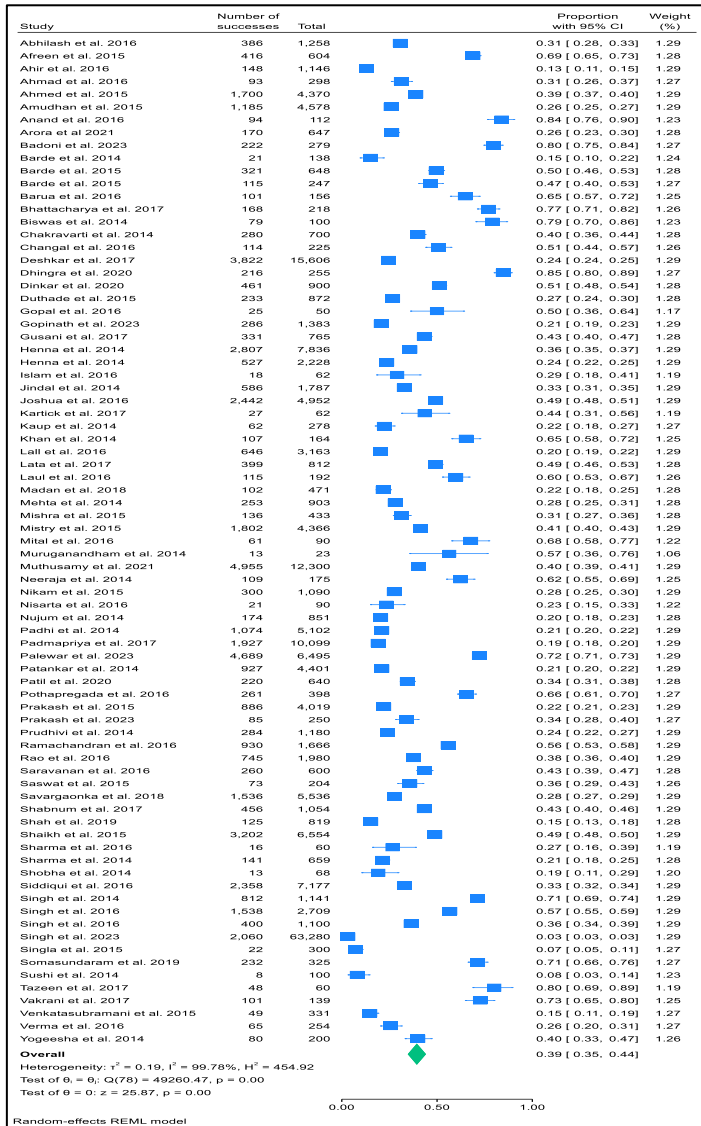


Figure 2: proportion (PP) of dg cases & OB

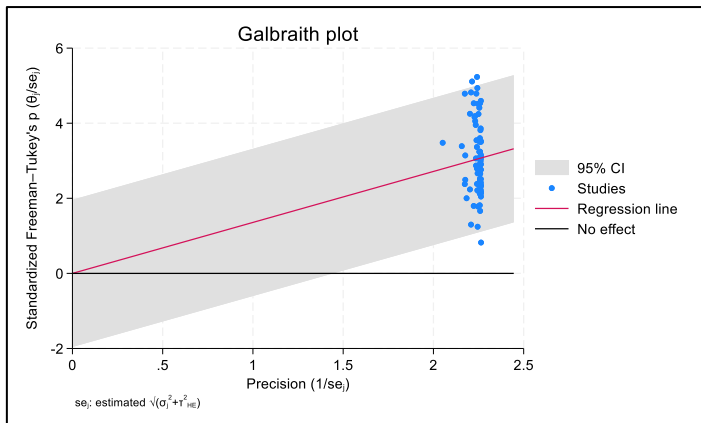


Figure 3: HITG analysis

Age distribution:

Data was available for 30 out of 127 studies on laboratory-confirmed DG cases. The overall average age of confirmed DG patients in this study was 24.47 years; with a standard deviation of 9.22 years with age range was 7 to 36 years as shown in Figure 4.

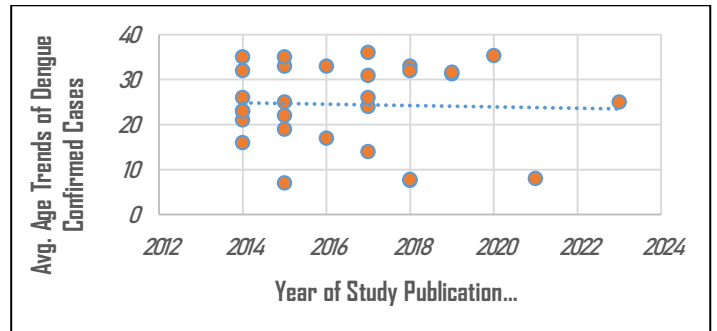


Figure 4: Age distribution (year-wise)

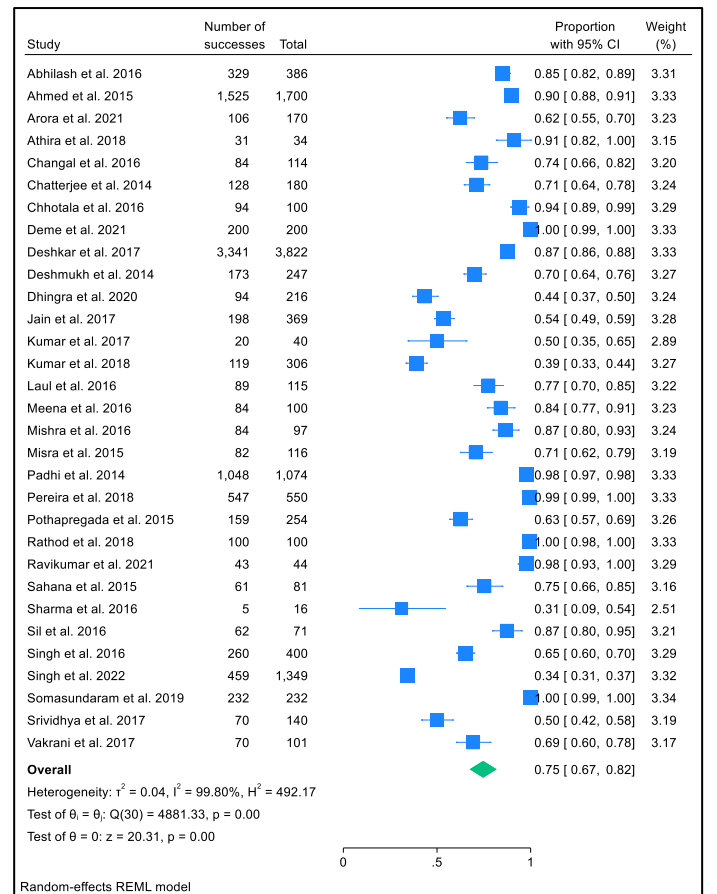


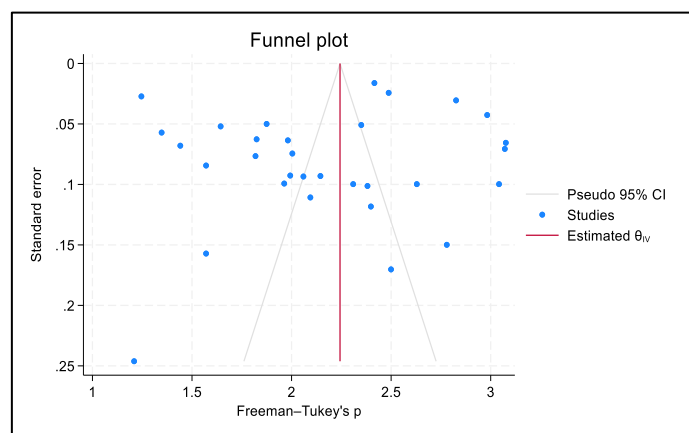
Figure 5: DG-FV-PP

Dg-FV & Dg-S proportion:

In the provided research, 31 studies provided information on DG-FV, while 32 studies provided information on DG-S. The majority of the research (n = 19, 59.38%) utilized the WHO 1997



classification, while the remaining studies ( $n = 3$ , 9.38%) employed the WHO 2007 classification. Additionally, for DG-FV condition and severity, ( $n = 6$ , 18.75%) used the WHO 2009 classification, whereas 4 studies (12.5%) used the WHO 2012 classification. It was reported that between 31% and 100% of laboratory-confirmed (LB-CN) patients had DG-FV. According to the REM, 75% (95% CI: 67-82) of LB-CN studies exhibited DG-FV overall. The Hedges  $g$ -Method (HD-M) was used to estimate the random effect model (REM), indicating no HTG as shown in **Figure 5**. Bias in publications observed and depicted that higher prevalence publications were more side. On the other hand, among patients with LB-CN, the reported percentage of DG-S cases varied from 2% to 69%. In the REM, the total percentage of DG-S across LB-CN studies was 25% (95% CI: 19-31). The data on DG-S showed no evidence of HTG as shown in **Figure 6**.



**Figure 6:** publication bias (PB-BA)

#### DG Mortality (MT) in India:

In the provided research, 48 provided information on MT rate of DG, It was reported that between 0% and 9% of LB-CN patients had DG-FV. According to the REM, 1% (95% CI: 1-2) of LB-CN studies exhibited DG-FV overall. The HD-M was used to estimate the REM, indicating no HTG. Bias in publications observed and depicted that higher prevalence publications was more side, The removal of the study with greatest weight in each LB-CN test of DG disease did not change the results.

#### Pm-if & SC among dg cases in India:

A comprehensive analysis of 15 studies [31, 37, 48, 59-60, 71, 78, 81-82, 89, 104-105, 115, 124] enabled the categorization of LB-CN-DG-IF into PM and SC. The prevalence of initial DG-IF varied widely ranges from 32% to 97% across the studies. Overall, PM-DG-IF accounted for 77% of LB-CN cases (95% CI: 65-87). Meanwhile, SC-DG-IF occurred in 23% of LB-CN cases (95% CI: 13-35), with a range of 3% to 68% across the studies.

#### PB-BA & sensitivity statistics (SS-ST):

There was no indication of publication bias in the dengue prevalence estimates from hospital-based studies with LB-CN cases, outbreaks & SP according to analysis utilizing funnel plots and the HD approach. The estimates of dengue severity and

fatality did, however, reveal a substantial publication BA, with publications demonstrating higher prevalence being more likely to be published. However, sensitivity analysis showed that the pooled percentages of research results held steady, suggesting the estimates' resilience. The removal of the study with greatest weight in each dengue cases LB-CN did not change the results.

#### Discussion:

The analysis primarily drew on data from HB and laboratory-based surveillance studies, as well as reports from investigations into dengue outbreaks. There have been more than 10 million reported cases of DG along with over 5,000 dengue-related deaths across 80 countries. The Pan American Health Organization (PAHO) region has reported the majority of cases, with over nine million cases. Within the PAHO region, Brazil has reported the highest number of cases (over eight million), followed by Argentina, Paraguay, Peru, and Colombia. In Europe, imported cases from endemic areas have been reported in Germany, Italy, and France, but no locally acquired cases have been reported. DG circulation has also been reported in the Southeast Asia and Western Pacific regions, as well as in Africa. It concentrated on their operations, implementation, and structure. The WHO had set aggressive goals to cut dengue-related mortality by 50% and morbidity by 25% along with burden by 2020 [135-136]. A recent study in Brazil found a significant disparity in the infection rates between wealthy and disadvantaged youth. Specifically, the study revealed that 60% of young people from disadvantaged backgrounds were infected, which is three times the rate of their wealthier peers and our study also found similar kind of results where average age was 24.4 years [137]. Overall, 127 studies with a total of 3Lacs population were covered for study of DG disease in our country. Viral assays are used in laboratories to confirm DG-IF (RNA detection by RT-PCR, NS1 antigen detection by ELISA) [138]. The overall prevalence of DG disease in our India based on testing of 206783 clinically suspected individuals from 79 studies, the overall estimate of the prevalence of LB-CN-DG-IF in the REM was 39.4% (95% CI: 35.6%-44.67%) According to a study, the overall prevalence of DG in country like India based on testing 206783 clinically suspected individuals from 79 different studies was 39.4% [139].

There are also research gaps in India's understanding of dengue epidemiology and the fact that different types of the dengue virus are still being spread. These factors show that dengue is still a major public health issue in India. The high percentage of dengue-positive cases, severity, and case mortality in India are all indicators that dengue continues to be a significant public health concern in the country. As a consequence of this, it is required to undertake community-based cohort studies that are well-structured and cover a variety of geographical locations of the country in order to offer reliable estimates of the age-specific incidence of dengue fever in India [140].

#### Conclusion:

DG-FV remains a pressing public health issue in India, as indicated by its high incidence, severity, and mortality rates, as well as the circulation of multiple virus serotypes. To better comprehend the epidemic, we suggest conducting in-depth research, including community-based studies across various regions to determine age-specific incidence rates. Alternatively, a nationwide survey could be undertaken to determine age-specific seroprevalence rates, which also includes targeted studies in different geographic areas in India.

#### Limitation:

- [1] We have restricted our search to quantitative sides which might be neglected towards qualitative enrichment of variables
- [2] We considered peer-reviewed journals database from certain articles, which lead to exclusion of government registries data as a grey literature that could provide other aspects of the picture too.

#### Future research:

We should implement active surveillance systems, scaling up vector control measures, enhance more public awareness & education and finally, strengthen the prevention strategies.

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