REPRODUCTIVE MORBIDITIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Dr. Ashok Kumar Dhanwal[1], Mr. Rajendra Kumar Sahu[2], and Mrs. Maitri Chaudhuri[2]*

Author[1] – Professor, College of Nursing Delhi, India.

Author[2] – Department of Nursing, Homi Bhabha Cancer Hospital and Mahamana Pandit Madan Mohan Malviya Cancer Centre Varanasi Uttar Pradesh (A unit of Tata Memorial Centre Mumbai, India).

Author[2]* & Corresponding author

Mrs. Maitri Chaudhuri

Principal, Nurses' Training Institute, Agartala Government Medical College and Govinda Ballav Panth Hospital, Agartala West Tripura, India, Email – maitrichoudhuridas@gmail.com

ABSTRACT

Background: Reproductive Tract Infections (RTIs), including Sexually Transmitted Infections (STIs), are silent epidemics, recognized as a public health problem, and rank second as the cause of healthy life loss among women of reproductive age. Objective: To assess the cumulative prevalence of reproductive morbidity & its associated factors focusing on comprehensive health care Design: Systematic review and meta-analysis of a community-based study. Data sources: PubMed (n=20), MEDLINE (n=7), Google Scholar (n=7), CINHAL (n=2), Scopus (n=1), others (n=8) and database. The literature searched was in the English language. The retrieval period was from January 2010 to May 2022. Study selection: Cross-sectional community-based study. Data extraction: All three authors independently screened the search results using titles and abstracts. Results: 6 studies were included in the systematic review and meta-analysis; the total sample subjects were 2,191 reproductive women aged 15 to 49 years. Prevalence rate among common signs and symptoms of 6 studies revealed that, vaginal discharge in two studies (107, 28.92 %, 117, and 71.34%), Irregular menstrual cycle (119, 36.6%), Genital discharge (126, 97.6%), frequent urination (43, 87.8%), abnormal vaginal discharge (39, 11.8%). Meta-analysis of all individual studies in CMA Software shows lower variation among the selected study. The Effect Size of the six studies was 0.157 in the Fixed Effect Model, 0.140 in Random Effect Model, and 95% CI. The small effect size shows that the difference between the studies is negligible, although it is statistically significant. the combined value of each 6 studies shows the Lower limit= 0.142 and 0.100, Upper limit= 0.173 and 0.193, Z-Value= -27.627 and -9.301, and p-Value= 0.000 and 0.000 which indicates highly significant at 95% CI. I^2 shows 89.8 the considerable heterogeneity among the selected studies. The combined variance of the six studies shows 0.022. The overall pooled random effect meta-analysis prevalence of reproductive morbidity was 0.140 (95% CI=0.100 – 0.193, I^2 =89.873, p=000). The 95 % confidence interval does not contain the null value, p-value <0.05; hence the differences observed in the study can be regarded as statistically significant. Conclusion: Awareness regarding available health services, especially the use of suitable contraception and the related benefits, has a greater influence on women's sexual and reproductive health status throughout their total lifecycle.

**PROSPERO ID No CRD42021229992, International prospective register of systematic reviews.*

Keywords: *Reproductive, Morbidity, Women.*

DOI Number: 10.14704/nq.2022.20.9.NQ44174 **Neuro Quantology 2022; 20(9):1508-1518**

INTRODUCTION

The concept of reproductive health has been used to define various health concerns relating to events that surround or affect human reproduction [1]. Women's health and their roles in health and development must be taken care of as maternal health affects the health of

the whole family, community, and thus society [2]. More than half a million women in the developing world die during pregnancy and childbirth due to preventable causes, with over 90% of those in Africa and Asia [3]. A woman carries a disproportionate and growing share of economic and domestic responsibility for the family. They are often regarded as financial burdens. These factors harm the health status of Indian women [4]. Reproductive Tract Infections (RTIs), including Sexually Transmitted Infections (STIs), are silent epidemics and are recognized as a public health problem and rank second as the cause of healthy life loss among women of reproductive age [5].

BACKGROUND

Indian women have high mortality rates, particularly during childhood and in their reproductive years. From a global perspective, India accounts for 19% of all live births and 27% of all maternal deaths (NFHS-3 data). Maternal injury and death, excessive blood loss, infection, high blood pressure, unsafe abortion, and obstructed labour are the most common direct causes and anemia, malaria, and heart disease are the most common indirect causes [6].

Terminating preventable maternal mortality must remain at the top of the global agenda. At the same time, simply surviving pregnancy and childbirth can never be the marker of successful maternal health care. Expanding efforts to reduce maternal injury and disability is critical to promoting health and well-being [6].

Sexual and reproductive health rights are fundamental for ensuring all women have access to respectful and high-quality maternity care[6].

Deaths caused by complications during pregnancy, childbirth, and the postnatal period have declined by 38 percent in the last two decades. Still, at an average reduction of just under 3 percent per year, this pace of progress is far too slow[6].

The Sustainable Development Goals (SDGs) offer a window of opportunity for the international community to work jointly and accelerate progress to improve maternal health for all women, in all countries, under all circumstances [7].

Commitment includes accelerating the progress in reducing newborn, child, and maternal mortality by ending all such preventable deaths before 2030 [7].

METHODS

The systematic review and meta-analysis proposal is based on the **PROSPERO, an International prospective register of systematic review** checklists. **Search Strategy:** The actual date for starting was 25/10/2020. The review stage includes Preliminary searches, piloting of the study selection process, and formal screening of search results against eligibility criteria.

Review question: What is the prevalence of reproductive morbidity? How can it be prevented? After a review of the literature on the Published study, a systematic search has been carried out in PubMed (n=20), Google Scholar (n=7), CINHAL (n=2), Scopus (n=1), and other databases (n=8). The literature searched was in the English language. The retrieval period is from **January 2010 to May 2022. PROSPERO ID No** CRD42021229992 **International prospective register of systematic reviews.**

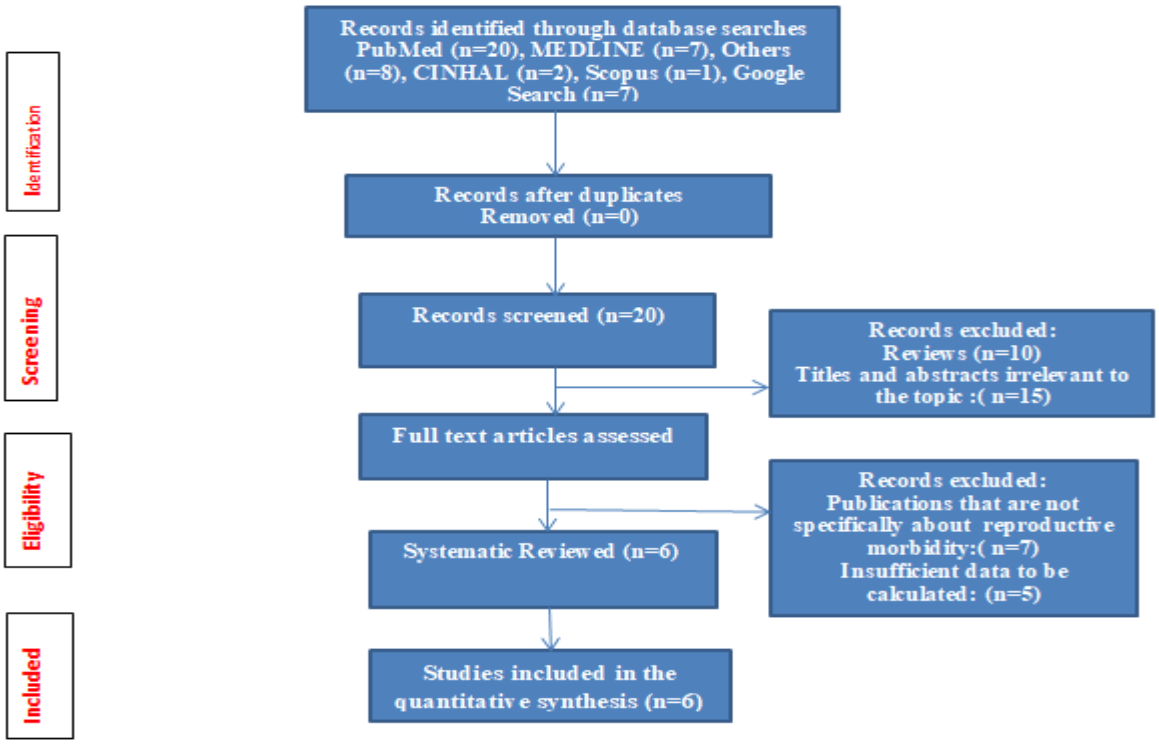

Figure: 1 Flow diagram of the search for eligible studies on reproductive morbidity among 15 to 49 years women.

Participants/population: Reproductive Age Group Women (15-49 years).

The protocol for the systematic review and meta-analysis is based on the PICO (population/intervention/control/outcomes) format, and PRISMA (Preferred Reporting Items for Systematic Review and Meta-analysis Protocols) 2015 checklist is used to prepare the research questions.

Table 1: PICO strategy, category, definition, and search terms in the database.

S.NO.	CATEGORY	DEFINITIONS	SEARCH TERM FOR GOOGLE
1.	Population	Reproductive age (15 to 45 years) group women	Reproductive morbidities
2.	Interventions	Interventions for reproductive age group women are designed to explore the behavior of the study participants	Available health services for Reproductive age group women
3	Control	-	-
4.	Outcomes	Reproductive health care, obstetrical care	Changes in Reproductive health status

SELECTION CRITERIA

Inclusion criteria

1) Community-based cross-sectional studies of reproductive age group (15-49) women.

2) Description of the socio-demographic characteristics of the respondents, reproductive morbidity, obstetrical histories, and methods of contraception used.

Exclusion criteria

1) Studies have a number of respondents less than 150.

2) Studies have incomplete data.

Context: Published research study conducted in the community setting to assess the prevalence of reproductive morbidity.

DATA EXTRACTION AND ANALYSIS

Data extraction

We have independently screened the literature based on search strategy, inclusion criteria, and exclusion criteria for extracting relevant data to accomplish the objectives. Thus, we reach the analysis solution.

- Name of Author
- Year of publication
- The setting of the studies
- Sampling method
- Data collection technique
- Sample size
- Prevalence of reproductive morbidity

Risk of bias (quality) assessment: All investigators thoroughly reviewed each study and resolved coding discrepancies. Abstracted data were then compiled, reviewed, and summarized in a table format, entered data of each study onto the evidence tables, checking and validating the information for accuracy. Risk of bias (quality) assessment was conducted using the quality evaluation tool of the Institute of Health Economics (IHE) case series methodological quality evaluation tool for evaluating eight areas of the literature. The selected four studies had more than 70% quality values, i.e. 75%, and were accepted quality.

Source: Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014. Available from: http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about.

Strategy for data synthesis: Statistical analysis:

The Statistical Analysis was conducted using CMA (comprehensive meta-analysis software). I^2 statistics are used to assess the heterogeneity among the studies. **According to the theory of Professor** Julian Higgins, **a rough guide to the interpretation of heterogeneity is like 0% to 40%: might not be significant, 30% to 60%: moderate heterogeneity, 50% to 90%: substantial heterogeneity, 75% to 100%: considerable heterogeneity**

Ethics and dissemination:

Ethical approval is not required because this review will draw on publicly available scientific literature. The findings of this systematic review will be published in a peer-reviewed journal, and updates will be made if there is new evidence that may cause any changes in the conclusions of the study.

Table 2: Screening of Selected Studies for Meta-Analysis

S.No.	Selected study	Author	Method of the study	Sampling technique, Sample size, method of data collection	Mean age of the study sample	Prevalence Rate
1	Reproductive morbidity profile among ever-married women (15-44) years of rural Etawah District, Uttar Pradesh: a cross-sectional study, 2016 (Study 1).	Vidya Rani1, Anand M Dixit Anand et al.	A cross-sectional study, rural area of Etawah district.	Multistage random sampling, **370,** **Interview**		**46.76%**
2	An Epidemiological study on morbidity pattern of women of reproductive age group (15- 45 years) in the peri-urban area of Tripura, 2018 (Study 2).	Kaushik Nag, et.al.	A community-based cross-sectional study, Sepahijala District, Tripura	**A random sampling of 325** house-to-house surveys,	**29.56 (**±8.68)	**82.2%**
3	A community-based study of reproductive tract infections among women of the reproductive age group in a rural community of Eastern India, 2018(Study 3).	Sulagna Das,et.al.	A community-based study of rural areas in West Bengal	Random sampling **312, Survey**	**28.06** ±8.2	**43.6%**

4	Prevalence of genital infections among women in reproductive age group in a rural area in North Kerala,2019 [study 4].	Enid, Elizabeth Thomas et.al.	Community-based descriptive study, rural area in Kannur district,	404, directly interviewing	32.20±10.7 41years.	52.7%
5	Reproductive tract infections in rural India – A Population-based study, 2019 (Study 5).	Vanitha Durai et. al.	**The population-based study**, Poonamallee Block at Thiruvallur district in Tamil Nadu.	Two-stage Cluster sampling method. **330,**	34.1 years	21%
6	An Assessment of Maternal Morbidity Pattern among Reproductive Age Group Women in a District of West Gujarat: A Community-Based Cross-Sectional Study,2018(Study 6).	Mittal Rathod	A Community Based Cross-Sectional Study, rural areas of Jamnagar district of Gujarat	Multistage sampling **450,** interviewing		80.0%

Table 3. Clinical signs and symptoms of the study participants

Sl. No.	Selected study	Signs and Symptoms	Prevalence rate
1	Study 1, n=370	Vaginal Discharge Lower abdominal Pain Menstrual Problems Pain/ burning micturition Vaginal Ulcer	Vaginal discharge (107, 28.92 %)
2	Study 2, n=325	Irregular menstrual cycle Dysmenorrhea Leucorrhoea Painful sexual intercourse (Dyspareunia) Uterine Prolapse Pelvic inflammatory disease Infertility Itching around genitalia (Pruritus vulvae) Burning sensation and or Pain during micturition (UTI)	Irregular menstrual cycle (119, 36.6%)
3	Study 3, n=312	Genital discharge Lower abdominal pain Itching Foul-smelling discharge Burning pain during micturition	Genital discharge (126, 97.6%)
4	Study 4, n=404	UTI (n=49): Fever, Burning urination, Frequent urination RTI *(n=164) Low backache, Excessive vaginal discharge	Frequent urination (43, 87.8%)

		Vulval itching, Lower abdominal pain Pain during intercourse, Foul smelling vaginal discharge, Altered consistency in vaginal discharge, Discoloured vaginal discharge, Genital ulcer	
5	Study 5, n=330	Abnormal vaginal discharge Itching in and around the genitalia, Burning in genitals, Dysuria, Lower abdomen pain (Pelvic Pain only), Decubitus ulcer in procidentia Dyspareunia, Genital ulcers, Low backache Inguinal swelling	Abnormal vaginal discharge (39, 11.8%)
6	Study 6, n=450	Vaginal Discharge, Abdominal Pain, Headache Vomiting, Oedema leg, Fever, Bleeding P/V Leaking P/V, Decreased fetal movement Visual disturbances, Oligohydramnios	Vaginal Discharge (117 71.34%)

Table 4: Meta-analysis of reproductive morbidity

S.No.	Selected Study	Sample size (n)	Common Signs and Symptoms	Prevalence Rate	Event rate	Logit Event Rate	Std Err	Variance
1	Vidya Rani, Anand M Dixit Anand et al.2016	370	Vaginal discharge	(107, 28.92 %)	**0.124**	**-1.952**	**0.158**	**0.025**
2	Kaushik Nag, et.al.2018	325	Irregular menstrual cycle	(119, 36.6%)	**0.252**	**-1.086**	**0.128**	**0.016**
3	Sulagna Das,et.al.2018	312	Genital discharge	(126, 97.6%)	**0.138**	**-1.834**	**0.164**	**0.027**
4	Enid, Elizabeth Thomas et.al.2019	404	Frequent urination	(43, 87.8%)	**0.129**	**-1.912**	**0.149**	**0.022**
5	Vanitha Durai,et.al.2019	330	Abnormal vaginal discharge	(39, 11.8%)	**0.064**	**-2.689**	**0.226**	**0.051**
6	Mittal Rathod,2018	450	Vaginal Discharge	(117 71.34%)	**0.178**	**-1.531**	**0.123**	**0.015**
Total	**6 studies**	**2,191**	**Common Outcome**					

A small variance indicates that the data points tend to be very close to the mean and each other.

	Study name	Subgroup within study	Events	Sample size	Event rate	Logit event rate	Std Err	Variance
1	ANAND et, al. 2018		46	370	0.124	-1.952	0.158	0.025
2	KAUSHIK NAG,		82	325	0.252	-1.086	0.128	0.016
3	SULAGNA DAS, et,		43	312	0.138	-1.834	0.164	0.027
4	ENID ELIZABETH		52	404	0.129	-1.912	0.149	0.022
5	VANITHA DURAI,		21	330	0.064	-2.689	0.226	0.051
6	MITTAL RATHOD,		80	450	0.178	-1.531	0.123	0.015
7								

Fig.2. Meta-analysis of Event rate and variance.

Model		Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	6	0.157	0.142	0.173	-27.627	0.000	49.371	5	0.000	89.873	0.202	0.148	0.022	0.450
Random	6	0.140	0.100	0.193	-9.301	0.000								

Fig: 3. CMA computation of Effect Size and heterogeneity.

Model	Study name	Statistics for each study					Event rate and 95% CI					Weight (Random)	Residual (Random)
		Event rate	Lower limit	Upper limit	Z-Value	p-Value	-1.00	-0.50	0.00	0.50	1.00	Relative weight	Std Residual
	ANAND et,	0.124	0.094	0.162	-12.389	0.000			+			16.71	-0.32
	KAUSHIK	0.252	0.208	0.302	-8.506	0.000			+			17.36	1.71
	SULAGNA	0.138	0.104	0.181	-11.164	0.000			+			16.56	-0.05
	ENID	0.129	0.099	0.165	-12.872	0.000			+			16.92	-0.23
	VANITHA	0.064	0.042	0.096	-11.323	0.000			+			15.00	-1.89
	MITTAL	0.178	0.145	0.216	-12.421	0.000			+			17.45	0.66
Random		0.140	0.100	0.193	-9.301	0.000			+				

Fig.4. Random Model analysis of Event Rate and 95%Confidence Interval.

Model	Study name	Cumulative statistics					Cumulative event rate (95% CI)					Weight (Random)
		Point	Lower limit	Upper limit	Z-Value	p-Value	-1.00	-0.50	0.00	0.50	1.00	Relative weight
	ANAND et,	0.124	0.094	0.162	-12.389	0.000						16.71
	KAUSHIK	0.180	0.086	0.339	-3.498	0.000						34.08
	SULAGNA	0.166	0.101	0.259	-5.578	0.000						50.63
	ENID	0.156	0.106	0.223	-7.518	0.000						67.55
	VANITHA	0.133	0.086	0.198	-7.645	0.000						82.55
	MITTAL	0.140	0.100	0.193	-9.301	0.000						100.00
Random		0.140	0.100	0.193	-9.301	0.000						

Fig: 5. Cumulative statistics of each selected study.

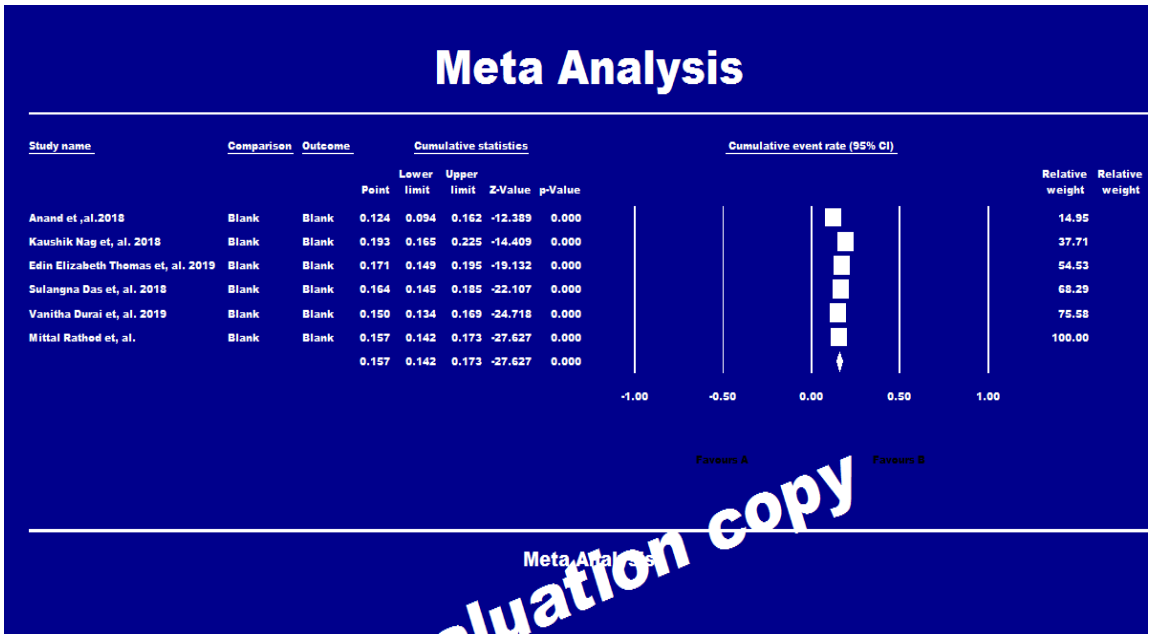

Fig: 6. The cumulative Evaluation copy of the meta-analysis shows the Forest plot of the selected study.

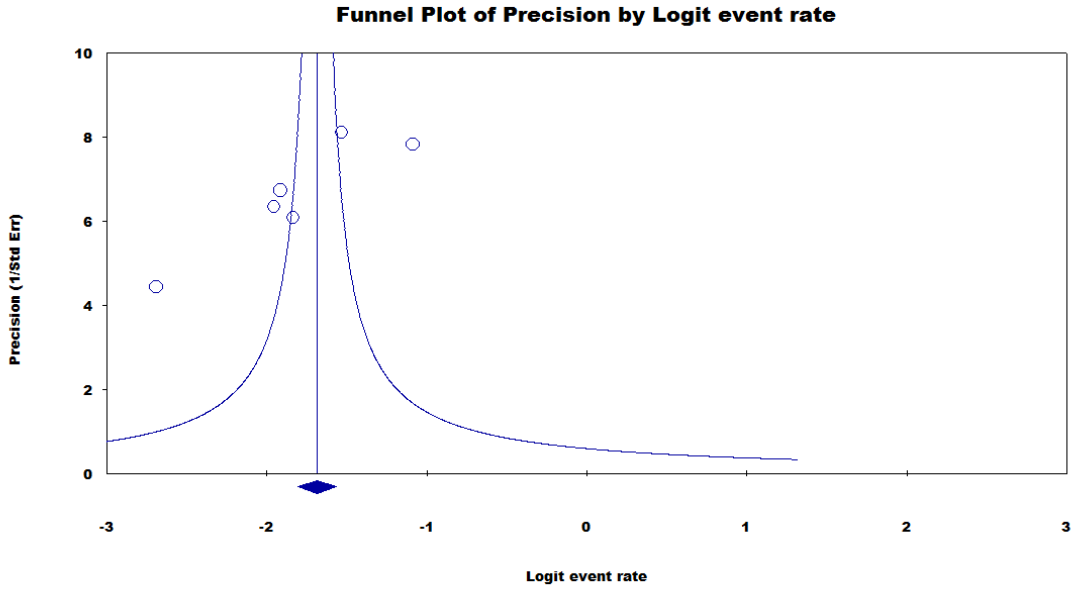

Fig. 7 Funnel plot to assess publication bias depending on the symmetry of the funnel plot

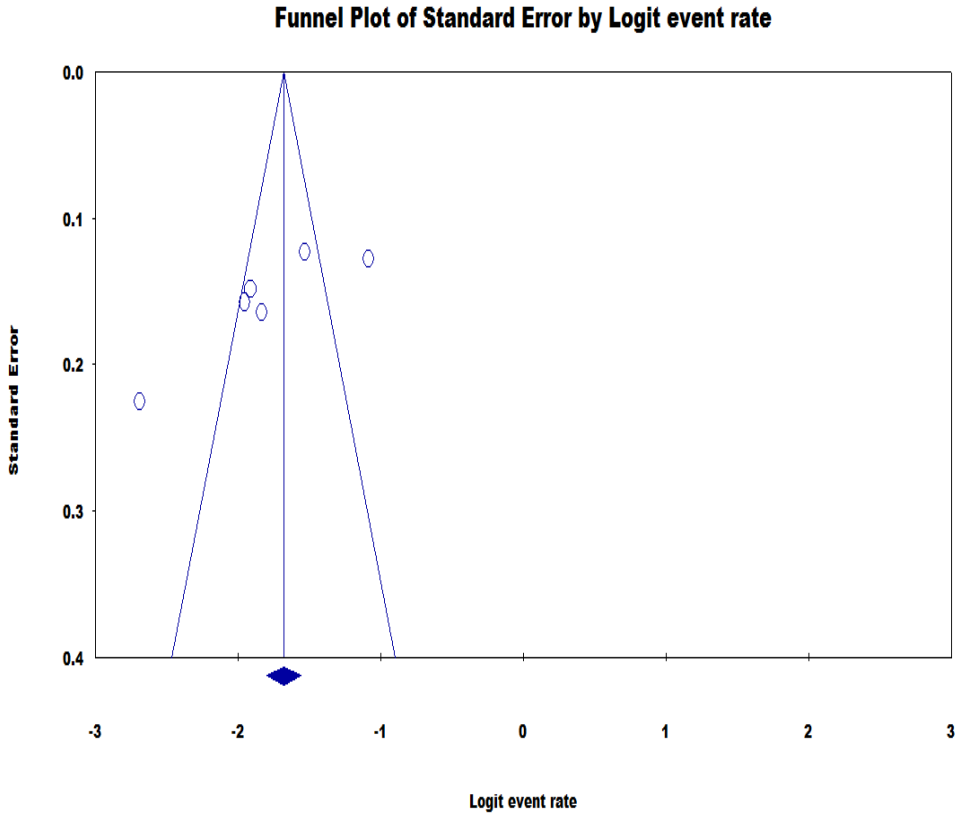

Fig. 8. Funnel plot to assess publication bias depending on the symmetry of the funnel plot.

Findings and Discussion: Overall total of 6 studies were included in the systematic review and meta-analysis [Table 2]. The result shows that the total sample subjects were 2, 191 reproductive women aged 15 to 45. Prevalence rate of 6 studies revealed that, common signs and symptoms were Vaginal discharge (107, 28.92 %), Irregular menstrual cycle (119, 36.6%), Genital discharge (126, 97.6%), Frequent urination (43,87.8%), Abnormal vaginal discharge (39, 11.8%), Vaginal Discharge (117 71.34%). [Table 3].

Meta-analysis of all individual studies shows when run in CMA Software, Event rate 0.124, 0.252, 0.138, 0.129, 0.064, 0.178, Logit Event Rate -1.952, -1.086, -1.834, -1.912, -2.689,-1.531, Std Err 0.158, 0.128, 0.164, 0.149, 0.226, 0.123, Variance among the 6 studies appeared as 0.025, 0.016, 0.027, 0.022, 0.051, 0.015. All are less than 1. It indicates that data points tend to be very close to the mean and each other. It determined the lower variation among the selected study [Table 4]. **Fig: 3.** shows the Effect Size of 6 studies I,e, 0.157 in the Fixed Effect Model, 0.140 in Random Effect Model, and 95% CI. The small effect size depicts the difference between the studies as negligible, although it is statistically significant. The combined value of each six studies shows the Lower limit of 0.142 and 0.100, Upper limit of 0.173 and 0.193, Z-Value = -27.627 and -9.301, and p- Value= 0.000 and 0.000, which indicates highly significant at 95% CI. I squared shows 89.8 is the considerable heterogeneity among the selected studies. It refers to the variation in study outcomes between the selected studies. A combined variance of the six studies shows 0.022. The overall pooled random effect meta-analysis prevalence of reproductive morbidity was 0.140 (95% CI = 0.100 – 0.193, I squared = 89.873, p = 000) [Figure 3 and 4]. The 95 % confidence interval does not contain the null value, p-value < 0.05; hence the differences observed in the study can be regarded as statistically significant [Fig.5]. This is a comprehensive analysis conducted to identify the prevalence estimation of reproductive morbidity among women of reproductive age (15 to 49 years) using meta-analysis. This comprehensive systematic review and meta-analysis of community-based studies conducted

in different parts of India included six reports and a 2191 women population. Hence, it provides a reliable estimate of the prevalence of reproductive morbidity. Major findings of our meta-analysis were Vaginal discharge (107, 28.92 %), Irregular menstrual cycle (119, 36.6 %), Genital discharge (126, 97.6%), Frequent urination (43, 87.8%), Abnormal vaginal discharge (39, 11.8%), Vaginal Discharge (117 71.34%). Cumulative random model meta-analysis of overall reproductive morbidity is 0.140 (95% CI = 0.100 – 0.193, I squared = 89.873,p = 000). Most study participants were under 20 to 24 years old and engaged in household activities. The healthcare-seeking behavior was deplorable. All the studies were community-based cross-sectional studies drawing sample populations by random sampling. The findings of our meta-analysis were consistent enough with the study findings of Dheresa M, Assefa N, Berhane Y, Worku A, Mingiste B, et al. (2017) [8]. They reported common gynecological morbidities were reproductive tract infection and menstrual disorders. Most women do not seek health care until it becomes an emergency. Reproductive morbidity was associated with illiteracy, ignorance, poor social status, lack of decision-making power, inability to seek health care, parity, early marriage, and age group. These findings are supported by Tehrani et al. BMC Public Health 2011 [9]. Their results revealed a high frequency of these morbidities and a culture of silence observed in the health-seeking behavior of women with ailments that need to be addressed appropriately in national health care screening programs.

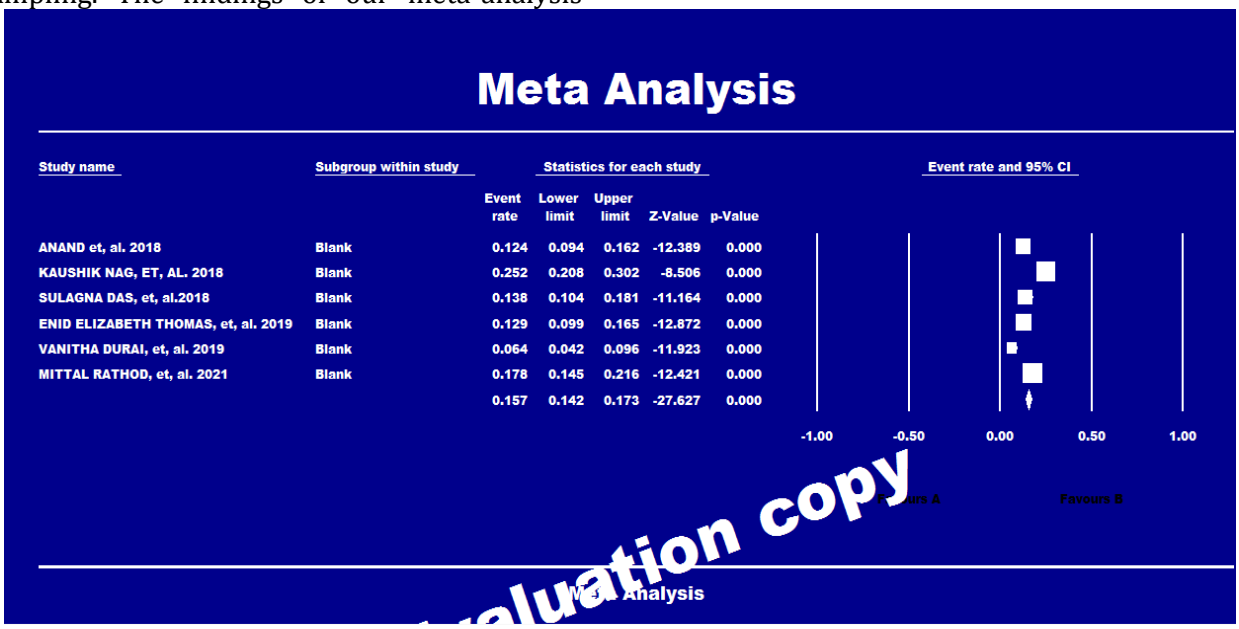

Fig.9. An evaluation copy of the meta-analysis shows the Forest plot of the selected study.

OVERALL REPRODUCTIVE MORBIDITY PREVALENCE

Overall reproductive morbidity prevalence was assessed. 4 studies represent Vaginal Discharge (389 women), 1 study Irregular menstrual cycle (119 women), and 1 study Frequent urination (43). A total of 2191 study populations were included in the overall pooled summary of meta-analysis prevalence.

PUBLICATION BIAS

Publication bias was evaluated by testing for funnel plot asymmetry. Each funnel plot appears asymmetry, which identifies a potential publication bias of all types of reproductive morbidities (Figures 7 and 8).

LIMITATION OF THE STUDY

Unpublished data did not include in this analysis, and thus publication bias likely may occur. The other limitation was that the papers included in this study were only papers written in English. This may also introduce Language bias and national health care screening programs.

Authors' Contributions: All the authors contributed to the writing, conceived and designed the paper, and performed the statistical analysis. All three authors read and approved the final manuscript.

CONCLUSION

Awareness of available health services and the related benefits significantly influences women's sexual and reproductive health throughout their total lifecycle. Prevention of reproductive morbidity and maternal and perinatal complications should include providing healthcare professionals with guidelines regarding the clinical management of complications to increase awareness among women about availing of health facilities.

Conflict of Interest

The authors declare that they have no conflict of interest.

REFERENCES:

1. Das S, Dasgupta A. Community-based study of reproductive tract infections among Women of the reproductive age group in a rural community of Eastern India. Int J Community Med Public Health 2019;6:330-6.
2. Mittal Rathod et al. Indian Journal of Community & Family Medicine | Vol. 4 | Issue 01 | Jan-Jun, 2018.
3. Kaushik Nag & Nabarun Karmakar., Sch. J. App. Med. Sci., Mar 2018; 6(3): 918-924.
4. Parsad K. Reproductive rights for women-Human rights issue. Social Welfare. 2002; 49(2): 20-23.
5. Rani V, Dixit AM, Kumar S, Singh NP, Jain PK, Peeyush K. Reproductive Morbidity Profile among Ever Married Women (15-44) years of Rural Etawah District, Uttar Pradesh: A Cross-Sectional Study. Ntl J
6. Community Med 2015; 7(1):35-40.
7. https://www.who.int/health-topics/maternal-health#tab=tab_1.
8. https://sdgs.un.org/2030agenda
9. Dheresa M, Assefa N, Berhane Y, Worku A, Mingiste B, et al. (2017) Gynecological Morbidity among Women in Reproductive Age: A Systematic Review and Meta-Analysis. J Women's Health Care 6: 367. doi:10.4172/2167-0420.1000367.
10. Tehrani, F.R., Simbar, M. & Abedini, M. Reproductive morbidity among Iranian women; issues often inappropriately addressed in health-seeking behaviors. *BMC Public Health* **11,** 863 (2011). https://doi.org/10.1186/1471-2458-11-863.