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## Does Insecticidal Treated Net Utilization Prevents Malaria A Systemic Review and Meta-Analysis

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### ABSTRACT

Malaria is one of the major public health problems worldwide affecting around 91 countries and territories. Use of insecticide-treated nets (ITNs) is one of the key components of malaria prevention and control as recommended by the World Health Organization (WHO). Thus, in this paper, we aim to summarize the evidence whether utilization of ITN is related to malaria illness through a systematic review and meta-analysis approach. Two investigators identified articles through data base searching of PubMed, SCOPUS, Google Scholar, Web of Science and MEDLINE from February 1 to February 26 2021. Two reviewers worked data extraction and quality assessment of studies. We include study if the study Newcastle Ottawa Scale score is 5 or greater. A random -effects model was used to estimate the pooled ORs with 95% CIs because there was evidence of heterogeneity. 13 studies comprising 6969 participants, 2187 of which had malaria illness were included in the quantitative syntheses (meta-analyses). The pooled odds ratios for all studies revealed no statistically significant association of malaria illness with ITN users relative to ITN non users OR 0.69 (95% CI 0.44 to 1.10),  $P = 0.12$ ,  $I^2 = 92\%$ ) There was significant heterogeneity for all studies ( $Q = 142.29$ ;  $P = 0.12$ ;  $I^2 = 92\%$ ). No publication bias was observed (Egger's test:  $P = 0.098$ , Begg's test:  $P = 0.329$ ). In this study the prevalence of malaria was low among those with ITN users than among those without ITN use (14.58% vs. 16.80%), although the difference was not significant. Thus, longitudinal studies are recommended in order to study peoples utilization behavior of ITN as well effectiveness of ITN in preventing malaria in the future.

**Keywords:** Insecticide treated net, Meta-Analysis, malaria, Systematic Reviews

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## INTRODUCTION

Malaria is a major public health problem worldwide occurring in 91 countries (1). Its etiology is a protozoan parasite of the genus *Plasmodium* (2-3). The disease is distributed in hot humid areas of Africa, Asia, and South and Central America. It also occurs in many temperate regions (4-6).

Globally about 3.2 billion people are at risk of malaria and 212 million cases were reported worldwide, with 429,000 deaths in 2015, particularly in sub-Saharan Africa and South Asia, Latin America and the Middle East countries.(7)

Since the early 2000s, malaria interventions have been scaled up in sub-Saharan Africa to control and eliminate the disease. The intervention includes distribution of long-lasting impregnated net (LLINs). The intervention has been successful to the reduction of malaria cases in many areas of sub-Saharan Africa. Despite this, there has been a resurgence of malaria in some areas [8-10].

A number of factors caused to the variations in malaria risks [11].

Some of the factors include use of preventive methods such as mosquito nets [12].

Use of insecticide-treated nets (ITNs) is a key component of malaria prevention and control as stated by the World Health Organization (WHO) [13].

Other factors such as bed nets availability, age and residence altitude, as well as household wealth, temperature, rainfall can affect malaria prevalence (14)

With the current sustained implementation of malaria control and prevention strategies across most African countries and the consideration of elimination in some settings [15, 16]

Documenting epidemiologic status of malaria and identification of its risk factors can help the decision makers to act timely to plan specific interventions

(17) This study aimed to determine the relationship between ITN utilization and malaria

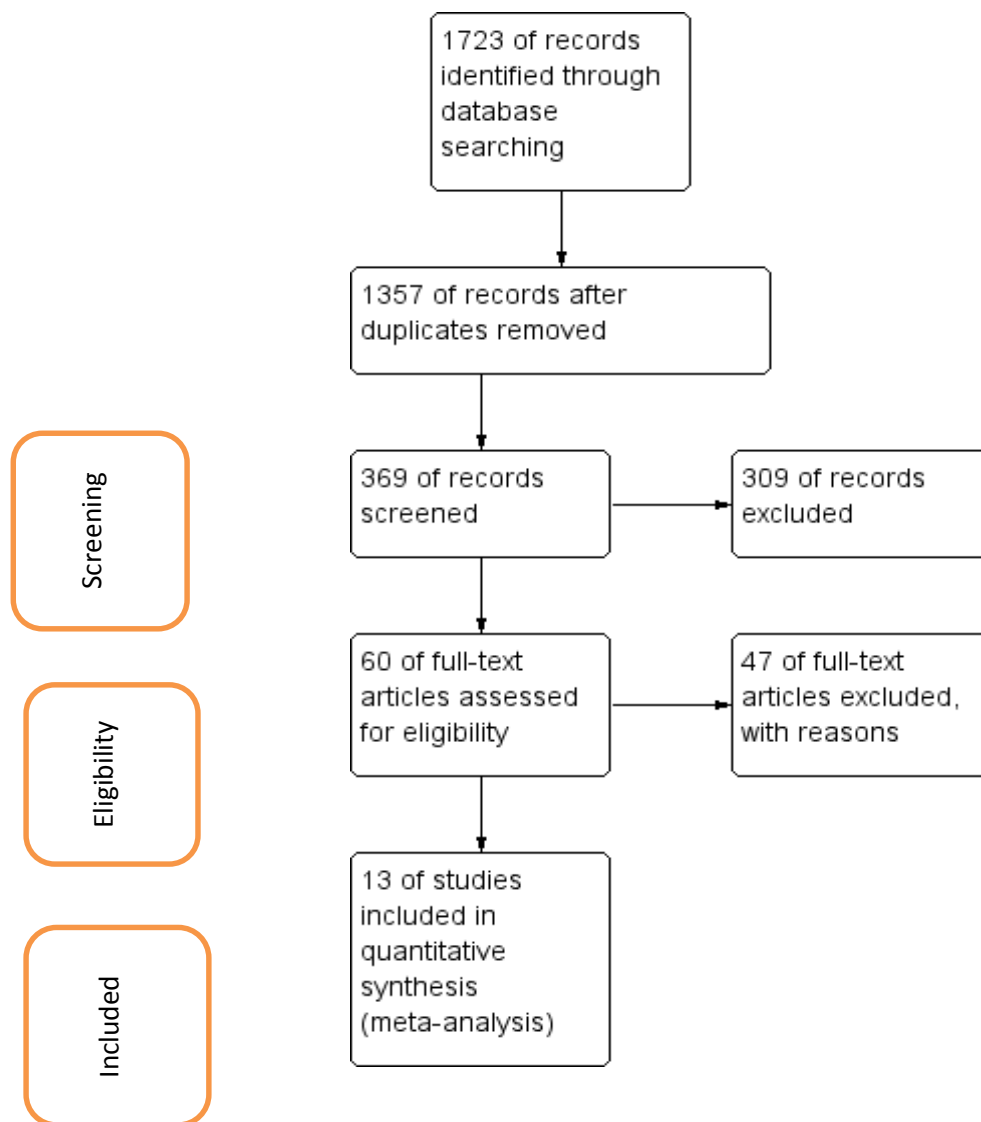
## MATERIALS AND METHODS

### Study design

This is a systematic review which includes a meta-analysis

Data Sources and Search Strategy

Identification



**Figure 1: PRISMA flow chart of the included studies selection process**

Review protocol does not exist since; we did not register in Cochran’s library. The PRISMA statement (18) for the reporting of systematic reviews recommended by the Cochrane Collaboration was followed while conducting this meta-analysis (see Figure 1).

Observational studies (cross-sectional studies, case control) on utilization of insecticide-treated net and malaria illness were included in our meta-analysis. Two investigators identified articles through data base searching of PubMed, SCOPUS, Google Scholar, Web of Science and MEDLINE from February1 to February 26 2021. Searches were performed using searching strategies of Boolean operator “AND”. For variable of “malaria” a combination of text words was used “factors associated”, “ITN” “insecticide-treated net”, “use of insecticide-treated net” was used.

### Inclusion and exclusion criteria

Studies were included in the review if; [1] the study design was cross-sectional study, case-control study, or cohort study, [2] the dependent variable was malaria , [3] the study reported number of malaria cases and utilization of insecticide-treated net in multiple logistics

regression analysis and [4] Newcastle-Ottawa Scale (NOS) score of 5 or greater indicated moderate- to high-quality studies (19)

Studies that were published not by English language were excluded

Two reviewers independently done identification of studies.

### Data Extraction and Quality Assessment

Two reviewers were worked data extraction and quality assessment of studies .The data extracted from selected studies was: first author's name, study design, source of study population, number of malaria cases, sample size and number of ITN users and non-users

All studies reported multivariable-adjusted odd ratios based on malaria. Therefore, we included findings that were controlled for confounding. Quality assessment was conducted using the ten-star Newcastle Ottawa Scale (NOS); see Table 2. We include study if the study NOS score is 5 or greater (19).After data extraction and assessment, the data on full text articles was checked by third reviewer

**Table 1: Description of original studies included (n=13), 2021**

Author / year	Sample size	Tittle / study design	Utes of ITN	Malaria	
				Yes	No
Abossie.A et al (20)	271	Prevalence of Malaria and Associated Risk Factors Among Febrile Children Under Five Years: A Cross-Sectional Study in Arba Minch Zuria District, South Ethiopia	Yes	10	139
			No	50	72
Tesfahunegn.A et al (21)	186	Risk factors associated with malaria outbreak in Laelay Adyabo district northern Ethiopia, 2017: case-control study design	Yes	46	102
			No	14	18
Ferreira .I et.al (22)	200	Factors associated with the incidence of malaria in settlement areas in the district of Juruená, Mato Grosso state, Brazil Cross-Sectional Study	Yes	7	16
			No	59	118
Essendi.W et al (23)	906	Epidemiological risk factors for clinical malaria infection in the highlands of Western Kenya case control study	Yes	146	390
			No	156	214
Wondimeneh.Y et al (24)	384	HIV and Malaria Infections and Associated Risk Factors Among Febrile Illness Patients in Northwest Ethiopia A cross-sectional study	Yes	213	58
			No	78	35
Mwalimu.C et al (25)	830	Factors Associated with Persistent malaria transmission in urban Peripheral Areas Dar es Salaam Region, Tanzania A cross-sectional population based survey	Yes	1	120
			No	3	17
Fana.S et al (26)	266	Prevalence and risk factors associated with malaria infection among pregnant women in a semi-urban community of north-western Nigeria cross sectional study	Yes	39	109
			No	67	40
Zgambo.M et al (27)	4040	Prevalence and factors associated with	Yes	301	876

		malaria parasitaemia in children under the age of five years in Malawi: A comparison study of the 2012 and 2014 Malaria Indicator Surveys (MISs) cross-sectional	No	301	695
Belete.E et al (28)	324	Malaria Prevalence and Its Associated Risk Factors among Patients Attending Chichu and Wonago Health Centres, South Ethiopia health institution based cross sectional study	Yes	41	38
			No	50	195
Alemu.G et al (29)	423	Asymptomatic Malaria Infection and Associated Factors among Blood Donors Attending Arba Minch Blood Bank, Southwest Ethiopia <i>An institution based cross-sectional study</i>	Yes	1	151
			No	16	248
Cahyaningrum.P et al (30)	96	Malaria Risk Factors in Kaligesing, Purworejo District, Central Java Province, Indonesia: A Case-control Study	Yes	40	25
			No	8	23
J-P GUTHMANN.et al (31)	1292	Environmental risk factors for clinical malaria: A case-control study in the Grau region of Peru	Yes	123	329
			No	200	637
U. Ezebialu.I et al (32)	390	Prevalence, pattern, and determinants of placental malaria in a population of southeastern Nigerian parturients cross-sectional study	Yes	48	41
			No	169	85

### Analysis of Data

The association between utilization of ITN and malaria illness was tested using number of malaria illness in ITN users versus ITN non users. A meta-analysis testing the difference in malaria illness among ITN users and ITN non users in 13 selected studies was done. The selected studies exhibit NOS quality assessment scores of moderate to high. Therefore, we did not performed sensitivity analyses according to NOS score and designated NOS scores from 5 to 6 as moderate and NOS scores equal to or greater than 7 as high. A random -effects model was used to estimate the pooled ORs with 95% CIs because there was evidence of heterogeneity (33) Forest plots were used to assess the OR estimates and corresponding 95% CIs visually. Heterogeneity between studies was evaluated using the Cochran's  $Q$  and  $I^2$  statistics (34,35). There was significant heterogeneity for all studies ( $Q = 142.29$ ;  $P = 0.12$ ;  $I^2 = 92\%$ ). The probability of publication bias was assessed using the Egger regression test (36) and Begg's funnel plot (37) No publication bias was observed (Egger's test:  $P = 0.098$ , Begg's test:  $= 0.329$ ). We analyzed data using Revman software (version 5.1) and Meta essential software. All statistical tests were two sided  $P$  value  $< 0.05$  was considered statistically significant

**Table 2: Characteristics of the included studies (n=13) according to Newcastle-Ottawa Quality Assessment Scale, 2021**

Study	Selection	Comparability	Outcome	NOS score
Abossie.A et al	***	**	*	6
Tesfahunegn.A et al	***	**	**	7
Ferreira .I et.ale	***	**	***	8
Essendi.W et al	***	***	***	9
Wondimeneh.Y et al	***	**	**	7
Mwalimu.C et al	***	**	***	8
Fana.S et al	***	**	***	8
Zgambo.M et al	***	**	***	8
Belete.E et al	***	**	**	7
Alemu.G et al	***	**	***	8
Cahyaningrum.P et al	***	***	***	9
GUTHMANN.J et al	***	**	***	8
I.U. Ezebialu et al.	***	***	***	9

**Note:** Each star represents a high-quality criterion accomplished by the study.

## RESULTS AND DISCUSSION

### Studies identified

A total of 1723 articles were identified through database searching. After removing duplicates, 369 studies remained. Screening these studies by titles and abstracts resulted in 60 studies that were assessed full text for eligibility. Of these, 13 studies were included in meta-analysis. The 13 studies consisted of 9 cross-sectional studies (20, 22, 24- 29, 32) and 4 case control studies (21, 22, 30, 31). The flow of studies through the review is depicted in Figure 1.

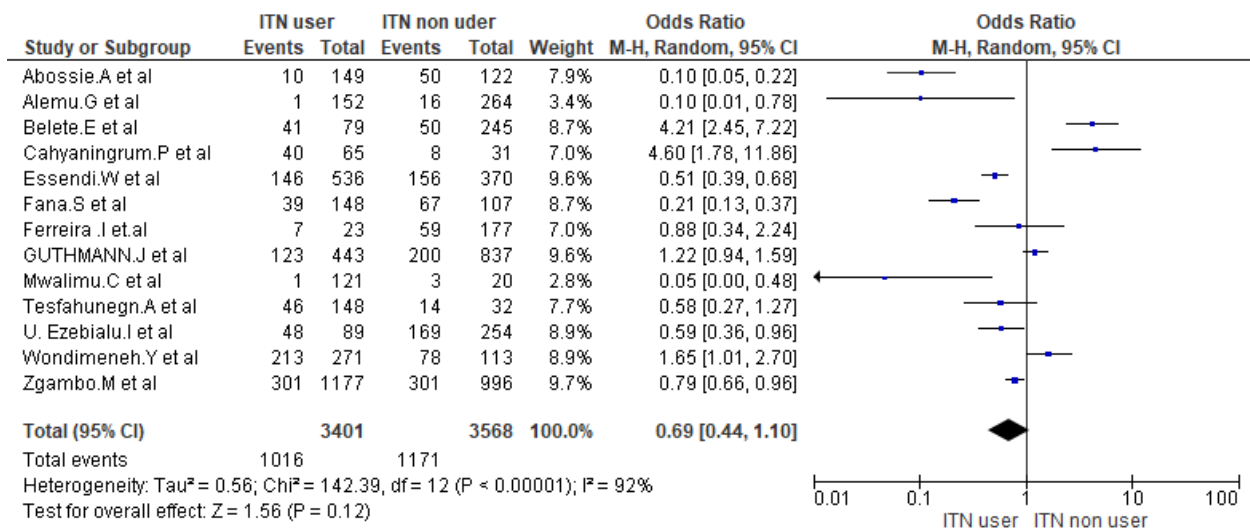
### Description of original studies

The total sample size of the 13 included studies comprised subjects (range, 96– 4040), (Table 1). 13 studies comprising 6969 participants 2187 of which had malaria illness were included in the quantitative syntheses (meta-analyses). All Studies asked utilization of ITN but the study populations differ that are Under Five Years:, Febrile Illness Patients,, pregnant women, Patients Attending Health Centers and Blood Donors Therefore, the studies varied in specific way.

### The association between utilization of ITN and malaria illness

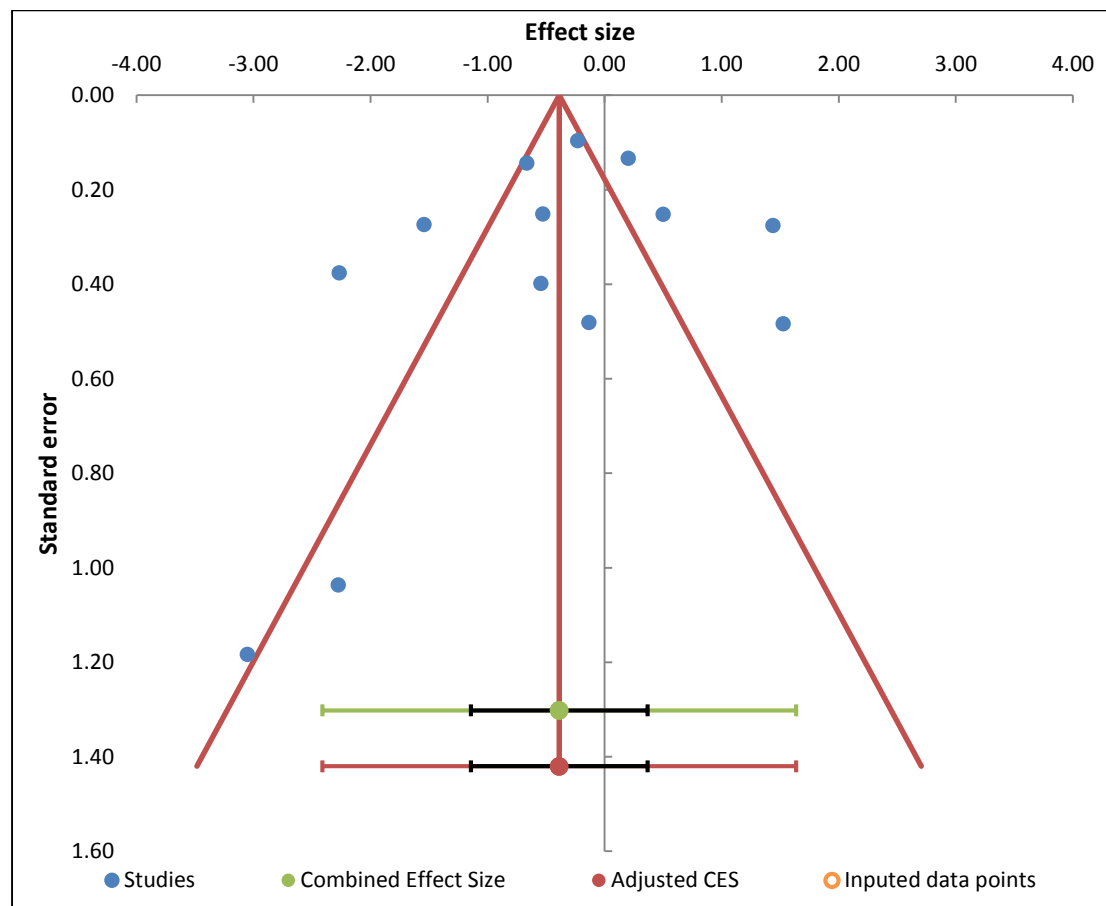
The pooled odds ratios for all studies revealed no statistically significant association of malaria illness with ITN users relative to ITN non users OR 0.69 (95%CI 0.44 to 1.10), P 0.12, I<sup>2</sup>= 92%) (Figure 2).





**Figure 2: Forest plot for the association between utilization of ITN and malaria illness**

### Publication bias analysis



### Egger Regression

	Estimate	SE	CI LL	CI UL
Intercept	-4.33	2.39	-9.54	0.89
Slope	3.71	2.29	-1.28	8.70
t test	-1.81			
p-value	0.098			

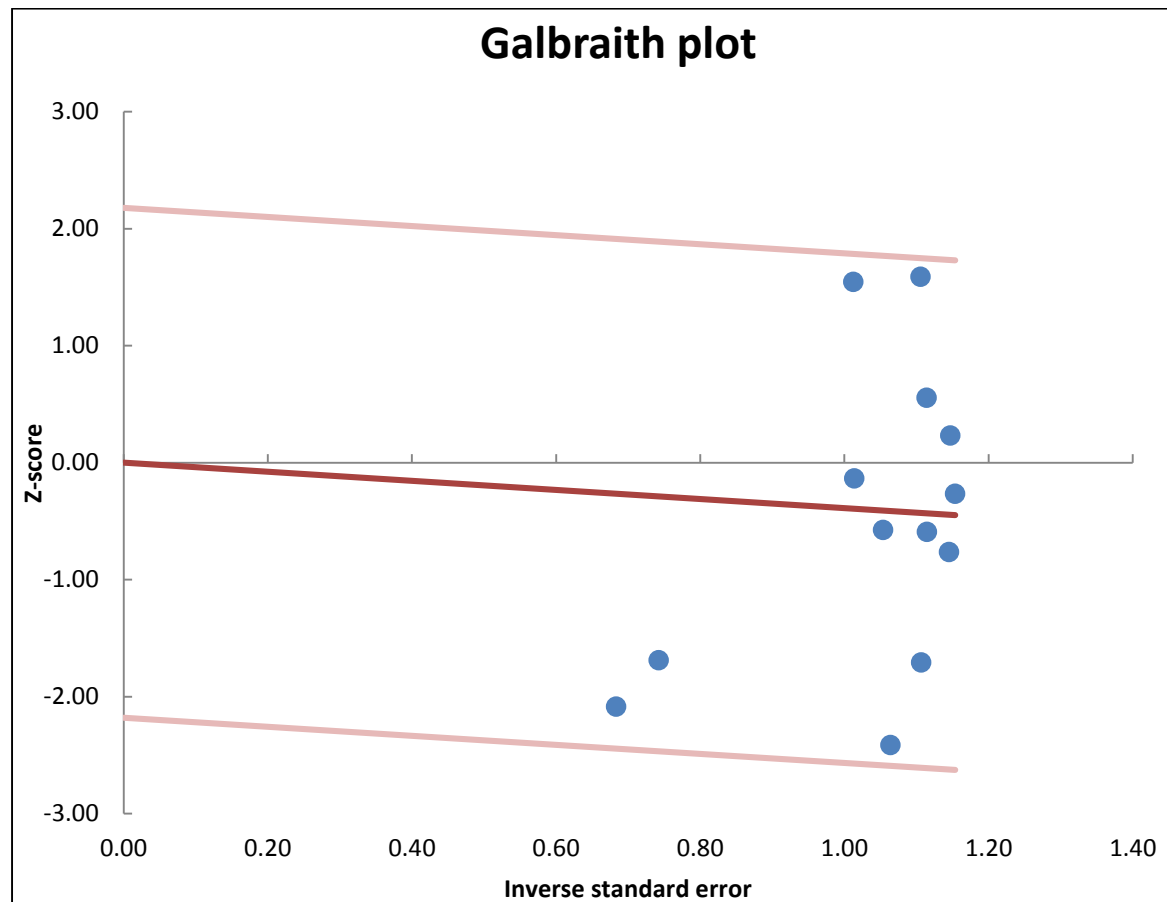
### Begg & Mazumdar

$\Delta_{x-y}$	-16.00
Kendall's Tau a	-0.21

z	-0.98
p	0.329

Figure 3 funnel plot for the Publication Bias Analysis of the association between ITN utilization and malaria

The Galbraith Plot can be used to look for outliers in the effect sizes. The expectation is that 95% of the studies is within the area defined by the two (lighter colored) confidence interval lines as the below plot show there is no outlier in the effect sizes



Regression estimate				
	Estimate	SE	CI LL	CI UL
Intercept	0.00			
Slope	-0.39	0.35	-1.14	0.37

Figure 4. Galbraith Plot for the Publication Bias Analysis of the association between ITN utilization and malaria

## DISCUSSION

According to the results of this meta-analysis, the pooled odds ratios for all studies revealed no statistically significant association of malaria illness with ITN users relative to ITN non users OR 0.69 (95%CI 0.44 to 1.10), P 0.12,  $I^2=92\%$ ).



This finding is consistent with previous studies which reported that insecticide treated net utilization was not significantly associated with malaria parasites (22, 23, 25, 27, 28, 31, 38, 39.).

A possible explanation for this finding might be underutilization of ITN, ITN may be torn, not impregnated recently and people may use ITN for another purpose in some areas like to harvest fish in Lake Malawi (40)

A previous study found that lack of knowledge on malaria affects compliance to LLIN use [41].

Future studies should consider assessing the relationship between knowledge on malaria and utilization of ITN.

In contrast, the finding of the study is inconsistent with previous studies which stated that those who did not use bed nets were more likely to be infected in Hadiya zone.(42), Indonesia (43), Uganda (44), Central India(45), Tanzania(46), Report of WHO (47), Nigeria[48]., Gambia (49) Nigeria (26)

The differences in the findings of our study and previous studies could be due to variation in type of ITN used since; the previous studies have been done with different type of ITN In addition, the variation might be due to differences in sample size, study population, study settings and climatic factors like topography, temperature, rainfall of study areas

Since our review include cross sectional studies and case control studies and without evidence of follow-up observation, the interpretation of results is limited concerning the utilization of ITNs

However, compliance with sleeping under a bed net must be a focus in addition to utilization of ITN

## CONCLUSION

In this study the prevalence of malaria was low among those with ITN users than among those without ITN use (14.58% vs. 16.80%), although the difference was not significant

Thus, longitudinal studies are recommended in order to study people's utilization behavior of ITN as well as effectiveness of ITN in preventing malaria in the future

## AUTHORS' CONTRIBUTIONS

Kaleab Tesfaye Tegegne was responsible for conceptualization, project administration, software, supervision, and development of the original drafting of the manuscript. Kaleab Tesfaye Tegegne, Andualem Zenebe, , Belayneh Feleke Weldeyes, Abiyu Ayalew Assefa, and Wosenyeleh Semeon Bagajjo were participated in quality assessment of articles, methodology, validation, and screening of research papers.

All authors contributed with data analysis, critically revised the paper, and agreed to be accountable for their contribution.

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