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Research article

Prevalence of clinical malaria and associated symptoms in pregnant women at Hamusit health center, Northwest Ethiopia

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ABSTRACT

Background: Malaria is the disease caused by intracellular parasites known as *Plasmodium* species and is mainly transmitted by blood sucking female *Anopheles* mosquitoes. During pregnancy, malaria results in severe complications to the mother, the fetus and the newborn. Symptoms of malaria, such as fever, malaise, headache, nausea and vomiting, in pregnant women can be mistakenly attributed solely to pregnancy. In Ethiopia, the prevalence of malaria in asymptomatic pregnant women has been well documented. However, studies indicating the prevalence and clinical presentation of malaria in pregnant women are lacking. Therefore, there is little information on the prevalence of malaria and significantly associated signs and symptoms in pregnant women. The aim of this cross-sectional study was to determine the prevalence of malaria and identify clinical signs and symptoms associated with malaria which suggest presence of malaria in pregnant women at Hamusit Health Center, Northwest Ethiopia.

Methods: A health facility-based cross-sectional study was conducted on 231 malaria symptomatic pregnant women from April to June 2023. A convenience sampling technique was employed. The socio demographic and clinical data of the study participants was collected through face-to-face interview using questionnaire. Thick and thin blood films were prepared from capillary blood and stained with 10 % Giemsa. The stained blood smear was washed with clean water, air dried and examined under a light microscope. The Statistical Package for Social Sciences software version 20 (SPSS 20) was used to analyses data. Logistic regression was used to assess signs and symptoms associated with malaria. An adjusted odds ratio with a 95 % confidence interval was calculated, and a P value < 0.05 was considered statistically significant.

Results: The overall prevalence of malaria among symptomatic pregnant women in the study area was 22.9 % (53/231) (95 % CI: 17.3–29 %). The most prevalent species was *P. falciparum,* with a frequency of 14.3 % (33/231) (95 % CI: 10 %–18.6 %), followed by *P. vivax,* 5.2 % (12/231) (95 % CI: (2.6 %–8.2 %). The remaining 3.5 % (8/231) (95 % CI: 1.8 %–6.7 %) were mixed infections of *P. falciparum & P. vivax*. Primigravidae (62.3 %) and first trimester pregnancies (52.8 %) were more affected. Malaria signs and symptoms mainly, fever [(P = 0.002, AOR (95%CI); 5.1(1.84,

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14.30)], joint pain [(P = 0.001, AOR (95%CI); 7.8(2.24, 27.32)], vomiting [(P = 0.007, AOR (95%CI); 2.9(1.34, 6.43)], malaise [(P = 0.005, AOR (95%CI); 3.6(1.48, 8.67)] and fatigue [(P = 0.0039, AOR (95%CI); 2.1(1.04, 4.37)], were significantly associated with malaria infection in pregnant women.

Conclusions: Malaria positivity in pregnant women with fever, joint pain, vomiting, malaise and fatigue is considerably high in the study area. These signs and symptoms in pregnant women are strong indicators of malaria infection.

1. Background

Malaria is the disease caused by intracellular parasites known as *Plasmodium* species. The 5 main species causing human malaria includes, *Plasmodium falciparum* (*P. falciparum*), *Plasmodium vivax* (*P. vivax*), *Plasmodium ovale* (*P. ovale*), *Plasmodium malariae* (*P.*) *and Plasmodium knowlesi* (*P. knowlesi*) [1].

In 84 countries where malaria is endemic, about 247 million cases and 619 000 deaths due to malaria have been reported in 2022, according to the World Health Organization (WHO) [2]. Of this worldwide burden, Africa accounts for 234 million cases (approximately 95 %) and 593 000 fatalities [2].

In Ethiopia, malaria transmission is usually different in different seasons and different areas. More than 66 % of the country's land is malarious and more than 60 million people areas are at risk of the infection [3,4]., Malaria in the country is primarily caused by *P. falciparum* and *P. vivax* with relative rates of 60 % and 40 %, respectively [5]. The primary malaria vector is *Anopheles arabiensis*, while minor vectors include *Anopheles pharoensis*, *Anopheles funestus*, and *Anopheles nili* [5]. More than 900 000 cases and over 200 deaths due to malaria have been documented in 2019 [6].

Pregnant women, especially primigravidae are at a significant risk of contracting malaria primarily due to *P. falciparum* [2]. There were an expected 40 million pregnancies in the 38 countries with moderate to high malaria transmission in the WHO African Region in 2021, of which 13.3 million (32 %) were exposed to malaria infection. The prevalence of exposure to malaria during pregnancy varies by WHO sub-region, with West Africa having the greatest prevalence (40.7 %), closely followed by central Africa (39.8 %) and eastern and southern Africa (20 %) [2].

Compared to non-pregnant women, pregnant women are three times likely to acquire malaria and have 50 % higher fatality rate [7]. They may be at higher risk due to factors including reduced immunity and the sequestration of infected erythrocytes to the placenta during pregnancy [8]. Moreover, even in the absence of data on their transmission potential, community chemotherapeutic programs aimed at reducing malaria transmission sometimes exclude pregnant women due to drug safety issues [8]. Despite this, pregnant women have higher potential of transmitting malaria due to their more attractive potential to *Anopheles* mosquitoes [9].

Malaria symptoms in pregnant women could mislead the diagnosis due to the development of similar manifestations because of pregnancy. Some malaria symptoms like fever, malaise, headache, and even gastrointestinal symptoms, such as nausea and vomiting, might be misinterpreted as pregnancy related symptoms [10]. Consequently, the lack of systematic clinical history-taking to rule out the possibility of malaria remains unresolved, leaving infected women untreated and resulting in serious maternal and fetal complications. In other words, such symptoms may lead to an incorrect diagnosis, such as influenza, gastroenteritis, typhoid fever, and encephalitis [10]. As result, it is critical to confirm malaria infection status and identify clinically significant signs and symptoms in symptomatic pregnant women. This will be important for prompt treatment and avoiding adverse pregnancy outcomes.

Pregnant women have minimal immunity to malaria in areas with low transmission, which makes infections more likely to be symptomatic and severe, leading to maternal and fetal fatalities if untreated [11,12].

The present approach of treating clinical malaria in pregnant women is based on the outcomes of microscopy or rapid diagnostic tests (RDTs) [13]. Despite the fact that the signs and symptoms of malaria in pregnant women have already been documented in a few settings [13–15], clinical presentation may vary depending on the rate of transmission and local perceptions. Therefore, identifying common signs and symptoms that are significant indicators of malaria infection in pregnant women is highly vital to identify those who require further diagnosis and confirmation by RDT or microscopy and prevent adverse outcomes.

In Ethiopia, the status of malaria in asymptomatic pregnant women has been well studied [16–19]. However, studies indicating the prevalence and clinical presentation of malaria in pregnant women are lacking. Therefore, there is little information on the prevalence of malaria and significantly associated signs and symptoms in pregnant women in the study area. As result, this cross-sectional study aimed to determine the prevalence of malaria and identify significantly associated clinical signs and symptoms suggestive of malaria in pregnant women at Hamusit Health Center, Northwest Ethiopia.

2. Materials and methods

2.1. Study design, period and area

A health facility-based cross-sectional study was conducted at Hamusit Health Center, Northwest Ethiopia, from April 1 to June 30, 2023. Hamusit is a town located 40 km north of Bahir Dar city. The area is situated 2077 m above sea level. The area has an average annual rain fall of 1300 mm and mean annual temperature of 26 °C (source: District agricultural office). Malaria transmission occurs year-round in the area, with the maximum intensity and rise in occurring seasonally September to November and May to July. Malaria

is the primary cause of morbidity and mortality in the area. Approximately 55 426 catchment populations receive health services from the Hamusit health center (Source: District health office). The area was thus selected purposefully because of the existing malaria burden throughout the year and logistic reasons.

2.2. Sample size determination and sampling technique

Using a single population proportion formula with 16.3 % prevalence [20], 95 % confidence level, 5 % margin of error and 10 % nonresponse rate, the final sample size was 231. Therefore, 231 pregnant women participated and were enrolled by a convenience sampling technique to achieve the sample size within the specified study period and with available resources.

Study population: The study participants were pregnant women (confirmed urine human chorionic gonadotropin (HCG) hormone positive in laboratory) [21] who exhibited at least one of the signs and/or symptoms of malaria, such as fever (axillary temperature as measured by electronic thermometer $\geq 37.5c^0$), joint pain, malaise, vomiting, and chills.

2.3. Dependent and independent variables

The dependent variable was malaria infection status. The independent variables were age, residence, educational status, occupation, gestational age, gravidity, signs and symptoms.

2.4. Operational definition

Clinical malaria: Pregnant women with symptoms related to malaria (fever [axillary temperature $\geq 37.5\ ^\circ C$], chills, malaise, joint pain, headache or vomiting) during examination.

2.5. Eligibility criteria

2.5.1. Inclusion criteria

Malaria symptomatic pregnant women who are permanent residents in the study area and gave consent to participate in the study were included.

2.5.2. Exclusion criteria

Pregnant women who have taken antimalarial drugs and antibiotics therapy with in the past one month before enrollment and unconscious during data collection were excluded.

2.5.3. Data collection

Clinical and sociodemographic data collection**:** During their visit to the health clinic, pregnant women who had malaria symptoms or signs were asked if they would be interested in participating in the study. The clinical and sociodemographic data of study participants were collected through face-to-face interviews by the Midwives using data collection tool (structured questionnaire). Questionnaire was prepared by reviewing previously conducted literatures and different malaria treatment guide lines.

2.5.4. Laboratory diagnosis of malaria

Blood sample collection: Capillary blood was drawn by competent and experienced medical laboratory personnels and the lead investigator for confirming malaria. The side of a pregnant woman's fingertip was pierced with a sterile lancet after being cleansed with 70 % ethyl alcohol. After wiping the first drop, 1 μl and 2 μl of blood were taken to prepare thin and thick blood films, respectively. After drying the smears with air and fixing thin films with absolute methanol, 10 % giemsa stain was added. It was then washed with clean water, dried with air and examined under 100x light microscope, air dried and. Minimum of 100 oil immersion fields were checked to report the result as Negative. Malaria infection status was reported as "positive" when the diagnostic stages (Trophozoites, Schizonts and Gametocytes) of the *Plasmodium* parasites were confirmed in blood films. Parasites were detected in thick films and species were identified with thin blood films.

2.5.5. Data quality control

Prior to collection, training was given to the data collectors on how to collect, recorded and store the collected data. About 5 % (12) of the questionnaires were pre-tested at Debre Tabor Comprehensive Specialized Hospital to ensure the quality of the data before starting collection. Gently filtered giemsa stain was mixed with buffered water of PH-7.2 for preparing working solution every 8 h to ensure quality of Giemsa. Laboratory investigation was done by two experienced microscopists. In case of discrepancy between the two microscopists (Positive/Negative), a third blinded reading was done. This was taken as the final result.

2.5.6. Data analysis

After checking completeness, the collected data were coded, entered, cleaned and analyzed using Statistical Package for Social Sciences software version 20 (SPSS 20). The variables were displayed and explained with descriptive statistics like frequency and percentage using tables and graphs. The clinical characteristics associated with malaria were assessed using logistic regression with adjusted odds ratios (AORs) at 95 % confidence intervals. Finally, variables with P value < 0.05 were considered statistically

significant.

3. Results

3.1. Sociodemographic characteristics of study participants

In total, 231 pregnant women with malaria symptoms took part in the study, with 91.3 % (211/231) of them living in rural areas. Among them, 84.8 % (196/231) were farmers, 71.9 % (166/231) were in the age range of 21–30 years old, and 77.1 % (178/231) were illiterate (Table 1).

3.2. Clinical data of the study participants

The primary symptom of malaria manifested by most of the study participants was fever (91.8 %, 212/231), followed by headache (188, 81.4 %) (Table 2).

3.3. Prevalence of malaria in symptomatic pregnant women

Malaria was confirmed in 22.9 % (53/231) of symptomatic pregnant women (95 % CI: 17.3–29 %) (Table 3).

3.4. Determination of malaria at gestational age and gravidity

Prevalence of malaria was higher among first-time mothers (62.3 %) and in the first trimester (52.8 %) (Table 4).

3.5. Frequency of signs/symptoms in malaria-infected pregnant women

The majority of malaria-infected pregnant women experienced joint pain (94.6 %), followed by fever (90.6 %) (Fig. 1).

Table 1
Sociodemographic characteristics of study participants (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

Variables	Category	Frequency (%)
Age group	≤20	28(12.1)
	21–30	166(71.9)
	31–40	37(16)
Residence	Rural	211(91.3)
	Urban	20(8.7)
Educational status	Illiterate	178(77.1)
	Primary	28(12.1)
	Secondary and above	25(10.8)
Occupation	Farmer	196(84.8)
	Private business	25(10.8)
	Employed	10(4.4)

Table 2
Clinical characteristics of study participants (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

Variable	Category	Frequency	Proportion (%)
fever	Yes	212	91.8
	No	19	8.2
Joint pain	Yes	175	75.8
	No	56	24.2
Headache	Yes	188	81.4
	No	43	18.6
dizziness	Yes	59	25.5
	No	172	74.5
Vomiting	Yes	144	62.3
	No	87	37.7
Malaise	Yes	14	6.1
	No	217	93.9
Fatigue	Yes	118	51.1
	No	113	48.9
Chills	Yes	140	60.6
	No	91	39.4

Table 3
Prevalence of malaria in symptomatic pregnant women (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

Result	Proportion %
Total positive	22.9 % (53/231); (95 % CI: 17.3 %–29 %)
P. falciparum	14.3 % (33/231); (95 % CI: 10 %–18.6 %)
P. vivax	5.2 % (12/231); (95 % CI: 2.6 %–8.2 %)
Mixed (*P. falciparum*& *P. vivax*)	3.5 % (8/231); (95 % CI: 1.8 %–6.7 %)

Table 4
Malaria prevalence at gestational age and gravidity in pregnant women (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

	Frequency		%
Gestational age	1sttrimester	28	52.8 % (28/53)
	2nd trimester	15	28.3 % (15/53)
	3rd trimester	10	18.9 % (10/53)
Gravidity	Primigravidae	33	62.3 % (33/53)
	Secundigravidae	14	26.4 % (14/53)
	Multigravidas	6	11.3 % (6/53)

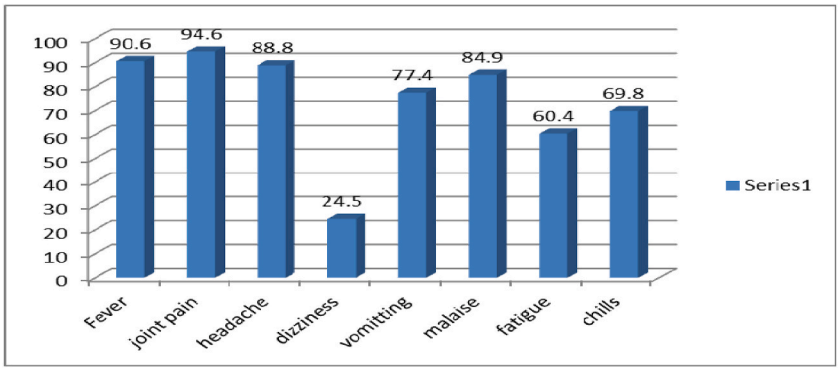

Fig. 1. Frequency of signs/symptoms in malaria-infected pregnant women (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

3.6. Signs/symptoms associated with malaria in pregnant women

Signs/symptoms with P < 0.2 in bivariate logistic regression were candidates for multivariate logistic regression. Malaria signs and symptoms mainly, fever [(P = 0.002, AOR (95%CI); 5.1(1.84, 14.30)], joint pain [(P = 0.001, AOR (95%CI); 7.8(2.24, 27.32)], vomiting [(P = 0.007, AOR (95%CI); 2.9(1.34, 6.43)], malaise [(P = 0.005, AOR (95%CI); 3.6(1.48, 8.67)] and fatigue [(P = 0.0039, AOR (95%CI); 2.1(1.04, 4.37)], were significantly associated with malaria infection (Table 5).

Table 5
Malaria associated signs/symptoms in pregnant women (N = 231) at Hamusit Health Center, Northwest Ethiopia, 2023.

Signs/symptoms	Category	Malaria		COR	P value	AOR	P value
		Positive	Negative				
Fever	Yes	48	122	4.4(1.66, 11.67)	0.003*	5.1(1.84, 14.30)	0.002*
	No	5	56	1			
Joint pain	Yes	50	125	7(2.11–23.66)	0.002*	7.8(2.24, 27.32)	0.001*
	No	3	53	1			
Headache	Yes	47	141	2.1(0.82–5.18)	0.126*	2.3(0.83, 6.25)	0.108
	No	6	37	1			
Vomiting	Yes	41	103	2.5(1.23–5.05)	0.012*	2.9(1.34, 6.43)	0.007*
	No	12	75	1			
Malaise	Yes	45	121	2.7(1.17, 5.99)	0.019*	3.6(1.48, 8.67)	0.005*
	No	8	57	1			
Fatigue	Yes	32	86	1.6(0.87–3.04)	0.125*	2.1(1.04, 4.37)	0.039*
	No	21	92	1			
Chills	Yes	37	103	1.7(0.87–3.25)	0.12*	1.5(0.68, 3.08)	0.331
	No	16	75	1			

4. Discussion

In areas of low transmission, pregnant women have less immunity to malaria. Malaria infection usually remain symptomatic and malaria in those women is more likely to become severe than non-pregnant adults living in the same area [11,12].

In this study, the prevalence of malaria was 22.9 % (53/231) (95 % CI: 17.3 %–29 %) which is in line with the result reported in Ghana (22 %) [21], Mali (28.1 %) [23] and Mozambique (26.3 %) [24]. However, our study result is lower than the study results conducted in Burkina Faso (49 %) [25]. This variation seems to be related to the difference in the overall prevalence and burden of malaria in Ethiopia and Burkina Faso. The frequency of malaria in Ethiopia is relatively lower than other endemic nations in Sub-Saharan Africa. However, Burkina Faso is among the top ten nations with malaria cases and deaths [26]. Moreover, this variation may be related to the variation in the length of study period and sampling technique. The present study was conducted in short period involving convenient sampling technique which might be potentially biased whereas, the study in Burkina Faso was follow up and case control nature [25].

In addition, the prevalence of malaria in this study is lower than the study result in southern Ethiopia (44.6 %) [27]. This difference might be due to the variation in inclusion criteria. For example, a study in Southern Ethiopia [27] was conducted in the Anti-Retroviral Therapy (ART) clinic among pregnant women who were confirmed HIV positive, which in turn increased malaria positivity and the severity of symptoms [28]. The magnitude and burden of malaria is higher in HIV infected pregnant women [28]. In addition, this study was conducted in both hospitals and health centers [27], where most pregnant women attend. However, the present study was conducted among pregnant women free of other underlying infections and in a health center. Most pregnant women attend hospitals for their ANC follow-up rather than health centers. In this case, the prevalence might be lower in health centers than in hospitals.

On the contrary, the prevalence of malaria in this study is higher than the study results reported in Pawe Hospital, (16.3 %) [20], and North Gonder, northwestern Ethiopia (11.5 %) [29]. This difference might be due to the difference in the study period. For example, our study was conducted in high malaria transmission season (April to June), where high prevalence and epidemics occur in the country. However, prior studies were conducted in seasons where malaria transmission is considered low (January to April [29] and October to May [20]).

Signs/symptoms related to malaria were more frequent in pregnant women in the study area, with joint pain (94.6 %) and fever (90.6 %) being the most commonly experienced. Analysis of signs/symptoms associated with malaria revealed that fever, joint pain, vomiting, malaise and fatigue were significantly associated with malaria infection. For example, pregnant women with fever, joint pain and vomiting were 5.1, 7.8 and 2.9 times more likely to have malaria infection, respectively, compared to pregnant women free of these signs/symptoms. Based on this finding, the presence of these signs/symptoms in pregnant women is indicative of malaria infection and alerts the need for early confirmation of malaria in health settings. This finding has been supported by similar findings in different studies conducted in pregnant women on malaria-associated symptoms and malaria positivity [22,24,26,30].

According to a study conducted in Mozambique [24], symptoms indicative of malaria were frequently occurring in pregnant women. In this study, about 77.4 % of pregnant women with clinical complaints of malaria had signs or symptoms indicative of malaria. Fever, arthromyalgia and a history of fever were the most common symptoms. The likelihood of having malaria was significantly increased in pregnant women with fever, headache, and shivering [24]. Similarly, fever and headache were significantly associated with having malaria infection in pregnant women according to the present study.

In another study conducted in Ghana [22], the association of signs and symptoms of malaria were assessed with peripheral parasitemia. Accordingly, malaria-infected pregnant women are often symptomatic. History of fever, headache, vomiting, general malaise, dizziness and fatigue were strongly associated with peripheral parasitemia. A similar study conducted in Burkina Faso [25], revealed that pregnant women were more likely to have malaria-related signs and symptoms. According to this study, most frequent and strongly associated signs and symptoms were fever, past history of fever, and headache. In another study, 90 % of malaria episodes in pregnant women studied in Benin [30], were symptomatic. In this study, fever, history of fever, headache and shivering had significant association with malaria infection.

Despite its effectiveness in many African countries, Intermittent Preventive Treatment with sulfadoxine pyrimethamine (IPTp-SP) is not implemented so far in Ethiopia [31]. The Ethiopian Ministry of health (MOH) does not support the use of IPTp with sulfadoxine-pyrimethamine due to relatively low prevalence of malaria transmission in most areas of the country, and the estimated minimal expected benefits compared with the relatively high costs of implementation. However, in many Sub-Saharan African countries, it remains effective even in low transmission areas [32,33]. Therefore, findings in the present study may be vital for considering the application of IPTp-SP policy in the country for preventing clinical malaria in pregnant women.

5. Conclusions and Recommendations

Malaria positivity of pregnant women with fever, joint pain, vomiting, malaise and fatigue is considerably high. These signs and symptoms in pregnant women are strong indicators of malaria infection. Therefore, health care providers should not always consider that such signs and symptoms are related only to pregnancy. Systematic clinical history taking to rule out the possibility of malaria and confirming the case in the laboratory should be considered. Malaria laboratory screening should be taken as part of routine laboratory test for every ANC visit to pregnant women. Moreover, case control-based studies incorporating extra signs and symptoms, knowledge of pregnant women on signs and symptoms and more sensitive and specific molecular techniques are recommended.

Limitation of the study

This is a cross sectional study without involving continuous follow up of patients for incorporating large sample size, extra signs and symptoms. Laboratory confirmation of malaria parasites was done only by microscopy without application of more sensitive and specific diagnostic techniques. In addition, the knowledge assessment of pregnant women on signs and symptoms of malaria was not performed.

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Ethical declaration

This study was reviewed by Department of Medical Laboratory Science, Debre Tabor University research review committee with the approval number (127/2023/). All participants/patients provided informed consent to participate in the study.

Data Availability statement

The data supporting the findings of this study are not deposited in to publicly available repository. The data used in this study are available from the corresponding author and will be accessible upon reasonable request.

CRediT authorship contribution statement

Andargachew Almaw: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mulat Yimer:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Megbaru Alemu:** Writing – review & editing, Supervision, Methodology. **Habtamu Belay:** Visualization, Investigation, Data curation. **Mihreteab Alebachew:** Visualization, Investigation, Conceptualization. **Getu Abeje:** Methodology, Investigation, Conceptualization. **Ayenew Berhan:** Writing – review & editing, Methodology. **Banchamlak Tegegne:** Writing – review & editing, Methodology, Investigation, Conceptualization.

Declaration of competing interest

In addition, we the authors affirm that this manuscript is original and neither submitted for publication nor published elsewhere in any language. Furthermore, all authors have read and approved the final version of the manuscript had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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