


# Mange Mites of Goats in Malle District of South Omo Zone, Southern Ethiopia

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**Background:** Mange mites are economically damaging goat ectoparasites that cause skin rejection or downgrading in Ethiopian tanneries and leather industries.

**Methods:** A study was done on 384 randomly selected goats to identify the proportion of mites and potential associated factors in the Malle district of South Omo Zone, Ethiopia using a cross-sectional survey. A questionnaire investigation was also performed to evaluate the knowledge and preventative measures taken by goat owners during mange mites infection. A skin scraping was employed to collect mange mites for identification.

**Results:** Out of 384 examined goats, 34.6% (133/384) of goats were infected with a variety of mange mite species. *Demodex* (2.86%), *Psoroptes* (8.1%), and *Sarcoptes* (23.7%) were the three mange mite genera identified in three sites of Malle district. Goats with poor body condition score (BCS) were the most infected (43.6%) with mange mites compared with moderate (39.1%) and good body condition (17.3%) goats. Adult goats (37.6%) were more infested than young (32.3%) and old (30.1%), whereas there was a higher infestation in males (60.2%) than females (39.8%). However, age, sex, and BCS of the goats had no significant ( $p > 0.05$ ) correlation with the occurrence of mange mites. Skin lesion due to mange mites infection was most frequently observed on the head region (26.3%), followed by legs (24.8%) and thoracic region (22.6%). The questionnaire survey indicated that 86.27% of the participants preferred to use modern acaricides to control mange mites, while 97.4% of participants have been involved in government-sponsored deworming programs.

**Conclusion:** Mange mites especially *Sarcoptes* species were major skin problems in goats in the study, so the owners should be advised to improve their management and use mite control in goats regularly in the area.

**Keywords:** mites, goats, Malle district, prevalence, South Omo Zone

## Introduction

Livestock farming in Eastern Africa is an important sector, which retains about 56% of African animal resources.<sup>1,2</sup> Goats are valuable species in large flocks for rural communities because they adapt to harsh conditions compared with sheep and cattle species<sup>3</sup> and are mainly kept by smallholder farmers across Ethiopia as a means of family income, milk, meat, and skins.<sup>4</sup> The skins of small ruminants, especially goat skins are well known for their quality.<sup>5</sup> Skins make up the second-largest generating field for foreign currency in Ethiopia, which produces 16.2 million pieces of export standard skin annually.<sup>4</sup> However, 35% of sheep and 56% of goat skins have deteriorated and are rejected in Ethiopian tanneries.<sup>6</sup>

Parasitic causes of skin diseases include sheep and goat pox, mange mites, ticks, lice, and fleas. They also depreciate the skin value and pose a major risk to skin

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export and livestock industries.<sup>7</sup> Among these, mites causing sarcoptic, psoroptic and demodectic mange, predominantly in the tropics, where favorable ecological conditions combined with poor husbandry could have a serious impact on development, are worth due attention.<sup>8,9</sup>

Mange causes allergic dermatitis due to infestations of mites, transmitted mainly through direct skin contact between animals.<sup>10</sup> Mange commonly occurs as discomfort and scratching-related skin conditions that lead to irritation, exudation, crusts, and scabs forming on the skin. If mites are left untreated, it results in loss of body condition and skin quality. Mange is mainly a problem of poor condition animals that commonly occurs during the winter season and has several clinical manifestations.<sup>11</sup>

Mange mite infections are a common problem of small ruminants globally as well as in the sub-Saharan area. The sources of infection include mites from clinically infected and carrier animals. Mange infection can occur during communal grazing, dipping, marketing, shedding, and overcrowding that facilitate rapid development of mite infestation.<sup>10,12,13</sup> Mange is characterized by several species-dependent clinical symptoms. Goat mites feed on the blood, lymph, skin waste, or sebaceous secretions they eat by piercing the skin, scavenging from the skin surface, or sucking from dermal lesions.<sup>14</sup>

Mange mites are the prevalent causes of clinical and subclinical skin conditions in small ruminants that occurs in various agro-ecological areas of Ethiopia.<sup>9,15–17</sup> The available studies in Ethiopia showed that mange mites in small ruminants belong to three main genera; *Sarcoptes*, *Psoroptes*, and *Demodex*.<sup>18</sup> Mange mites are commonly widespread in goat and sheep of Kombolcha district of the Amhara and also seen Oromia province.<sup>18,19</sup>

*Sarcoptic* mange (*Sarcoptes scabiei*) is caused by burrowing mites causing extreme pruritus, scratching and rubbing against inanimate objects. Constant scratching results in restlessness and affects the time spent to take food and degrades the consistency of the skin. *Psoroptic* mange (*Psoroptes cuniculi*) is induced by non-burrowing mites that feed superficially on lipid emulsion of skin cells and exudates and trigger a hypersensitivity reaction to the existence of fecal material from the mites. This exposes the infected animal to extreme pruritus, loss of wool, restlessness, infested areas being bitten and scratched, weight loss, and death in some instances. *Demodectic* mange (*Demodex caprae*) is found deep in the skin and causes pustules, redness, scaling, nodules, and hair loss.<sup>14</sup>

Skin scraping is commonly used for diagnosis of dermatological conditions such as mange infection. The blade is dipped in drops of mineral oil before scratching the skin. The skin is deeply scraped for burrowing mites until the capillary fluid oozes out.<sup>20</sup> Mange causes great financial loss to farmers due to livestock death, poor production and reproduction performance. It is also an important factor for downgrading or refusal of the skin of mange-infested animals in the tannery.<sup>11</sup> Besides, the effect of the disease on skin damage severely limits the tannery plants' performance that also limits the foreign currency earnings of the country.

There are few studies and reports on mange mites infestations of small ruminants in the country, regarding the main potential factors for infections, such as differences between age and species vulnerability to mite infestation and association with a specific agro-ecology. Very few scientific studies have taken place due to the remoteness of the area and most of the livestock species in the region have yet to be studied.<sup>21</sup> Mange infestations in the Malle woreda are prevalent in small ruminants; their distribution, identification of species, and associated risk factors for mange have not been adequately studied in the district. This research was performed to determine the occurrence and the associated risk factors for mange mites in goats in Malle district of the South Omo Zone.

## Methods

### Study Area

The research was conducted in selected districts of Malle, namely Bulansa, Kalendo, and Arkiroko, located in the South Omo region and its capital, Lemo-Gento, 819 km from Addis Ababa, 577 km from SNNPR, and 97 km from South Omo. Malle district covers the area between 5°01'–5°73'N and 36°38'–37°07'E. Regarding agro-climatic zone subdivision, 46% of the total 2922.8 sq. meters of Malle district land falls under Bertha, and 53.5% falls under lowland (Kola) and only 0.5% of the site is under Midland (Woyina dega). Although the mean annual rainfall of the woreda is 1000 mm, it is simply an average and is not be a good representative of rainfall amounts of wide areas in the woreda such as Kollo, Doiso, Bobo that get less than 500 mm of annual precipitation. Data recorded in the woreda indicate that the daily temperature varies between 30°C and 35°C and that the altitude varies between 500 and 2500 meters above sea level. In general, the topography of the woreda is flat to gently sloping,

although some undulating and mountainous areas contribute to a very small fraction of the woreda's total livestock population. The woreda has a total of 372,545 cattle, 482,118 goats, 109,780 sheep, 16,656 donkeys, and 112,475 poultry.<sup>22</sup>

## Study Animals

Indigenous goats, owned by farmers in different sites of the district, were investigated in this study. All the goats that were kept under free grazing were considered during the study period.

## Study Design

A cross-sectional survey was undertaken from September to April 2020 in three selected sites of Malle district, South Omo namely Bulansa, Kalendo, and Arkiroko. The presence/absence of any one or more species of mange mites in an animal was included in the current study. Mange mite status in animals of both sexes, various age groups, and animals with various body conditions were documented. The body condition score and age of the sampled goats were determined according to the standards set by Steele<sup>23</sup> and Russel.<sup>24</sup> The ages of the goats were determined based on their dentation and classified into three groups; young (< 2 years), adult (2–4 years), and old (> 4 years).<sup>25</sup>

## Sample Size Determination

The number of sampled goats were calculated using the Thrusfield<sup>26</sup> formula with 50% expected prevalence; a 5% desired absolute precision, and a 95% confidence interval.

$$N = \frac{1.96^2 p_{exp} (1 - p_{exp})}{d^2}$$

Where n = required sample size, Pexp = expected prevalence, d = desired absolute precision. Hence, 384 goats were selected for this research.

## Study Methodology

### Sample Collection Techniques

A total of 384 samples were collected from the skin of selected goats. Clinical examination was focused on the hair and visual inspection and palpation of the skin for lesions on all parts of the goats including the head region, the neck, thorax, flanks, rump, tail, and legs. Goats with signs of erythema, pruritus, and scale or crust formation were considered.

Skin scrapings samples were collected from active lesions by cutting the hair, and scraping the edges of the active lesion with a blade until blood oozed out. In addition to the skin scrapings, hair samples were collected and transferred to a labeled tube containing glycerin for further parasitological investigation.<sup>27</sup>

### Parasitological Examination and Morphological Identification of Mange Mites

The samples were digested for 30 minutes in a 10% potassium hydroxide solution before being analyzed under a light microscope.<sup>28</sup> Skin scrapings were taken for different mange mite species, and species identification was done using taxonomic morphological key characteristics according to Wall and Shearer<sup>29</sup> and Taylor et al.<sup>14</sup>

### Questionnaire Survey

A semi-structured questionnaire was created to gather information on the general stance of each goat owner and to determine care and prevention procedures for mange mite infestation and assess the risk factors for disease incidence. From three peasant associations (sites), a total of 153 goat owners (51 persons from each site) that brought animals for regular vaccination were randomly selected and interviewed. The questionnaire sample includes points such as the purpose of keeping goats, affected age group, seasonality, and control practices ([Supplementary File](#)).

## Data Analysis

Data gathered from the field and laboratory assays were recorded in Microsoft Excel spreadsheet 16 and analyzed using STATA version 13 statistical software. The correlation between occurrence of mange mites and possible putative factors were analyzed via the Chi-square test. Statistically significant correlation was considered at  $p < 0.05$ .

## Ethics Approval and Consent to Participate

The Animal Research Ethics Review Committee of Wolaita Sodo University granted ethical approval for the collection of mite samples from goats. During skin scraping and the questionnaire survey, all required permissions were obtained from each site's administration and agricultural office, as well as from each goat owner.

# Results

## Mange Mites Prevalence in the Goats of Malle District

In the current study, 34.61% (133/384) of the goats tested positive for mite infection in the Malle district. According to the present study, three types of mange mite genera were identified in three sites of Malle district with prevalence rates of *Demodex* 11 (2.86%), *Psoroptes* 31 (8.1%), and *Sarcoptes* 91 (23.7%) (Figure 1).

The degree of mange mite infestation in the three agro-ecological sites revealed that *Sarcoptes* was the most common mange mite genus identified in Arkiroko, 21 (23.08%), Bulansa 36 (39.56%), and Kalendo 34 (37.36%) followed by *Psoroptes* [Arkiroko, 10 (32.26%); Bulansa, 11 (35.48%); and Kalendo, 10 (32.26%)] and *Demodex* [Arkiroko, 4 (36.36%); Bulansa, 4 (36.36%), and Kalendo, 3 (27.27%)]. There was no significant correlation ( $p > 0.05$ ) between the occurrence of mange and the three study sites (Table 1).

## The Impact of Risk Factors in Prevalence Mites

In this study, male goats (60.2%) were more infested with mange mites than female goats (39.8%). Thus, sex has a significant correlation ( $p = 0.0001$ ) with the occurrence of mange infection. Whereas, a higher prevalence of mange mite infestation was registered in adults (37.6%) as compared with young (32.3%) and old (30.1%). Based on their body condition score, the higher prevalence was observed in poor body condition (43.6%) followed by moderate body condition (39.1%) and good body condition (17.3%); however, there were no significant correlation between the frequency and factors such as age, and body condition (Table 2).

## Distribution of Mites in Different Body Parts

In the present study, mange mite lesions were detected at the highest frequency from the head region (26.32%), followed by the leg region (24.81%) and the thoracic region (23.5%), whereas the flank region was less infected (0.8%). There was a statistically significant ( $X^2=384$ ,  $p = 0.0001$ ) association between the mange mite lesions in the different parts of the body (Figures 2 and 3).

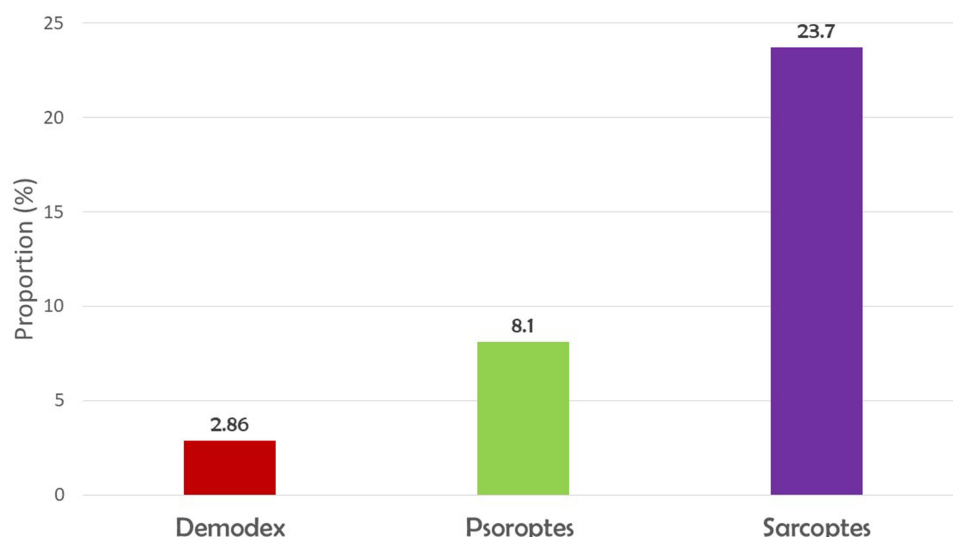
## Questionnaire Survey Output on Different Factors Related to Mange Mite Infestation

In the current study, the questionnaire survey showed that 85.66% (128/153) of the respondents in the three sites of Malle district rear goats for generating revenue whereas 16.33% (25/153) keep them for household meat and milk consumption. The present study revealed that 42.5% (65/153) of the respondents explained that adult goats were more affected than old, 37.91% (58/153), and young goats, 19.6% (30/153). Additionally, 85.62% and 14.3% of the participants replied that the mange infection was a more serious problem during the dry season than wet season, respectively (Table 3).

Moreover, 86.27% (132/153) of the participants used modern treatment options (ivermectin 1%, injection and dipping/spraying using acaricides) and 13.73% (21/153) replied that traditional treatments (ethnomedicines) are also used as a management option. Moreover, interviewed individuals explained that among ectoparasites, parasites such as mange mites, 98 (64.05%), ticks, 38 (24.83%), and lice, 17 (11.11%), were the dominant cause of skin diseases that commonly occur in these three sites of Malle district. Regarding the control strategies, 149 (97.4%) respondents were involved in a control program provided by the government (Table 3).

**Table 1** Prevalence of Mange Mites in the Three Sites of Male Districts (N = 384)

Genera of Mange Mites	Sites N (%)			$X^2$	p-value
	Arkiroko	Bulansa	Kalendo		
<i>Demodex</i>	4(36.36)	4(36.36)	3(27.27)	6.28	0.393
<i>Psoroptes</i>	10(32.26)	11(35.48)	10(32.26)		
<i>Sarcoptes</i>	21(23.08)	36(39.56)	34(37.36)		



**Figure 1** Prevalence of mange mites in the three sites of Malle district.

## Discussion

The present survey revealed that the prevalence of mange mites infection in goats of Malle district was 34.6%. The finding of the present study was higher than the previous results of Fekadu et al.,<sup>30</sup> 25.7% in three agro-ecological zones (Chencha, Lanfro, and Benatsemay), Yasine et al.,<sup>9</sup> 13.8% in Oromia Zone of Amhara Regional state, Zeryehun, and Mengesha,<sup>31</sup> 11.7% in Kombolcha; Zeryehun and Tadesse,<sup>32</sup> 9.24% in Nekemte Veterinary Clinic, Mandado et al.,<sup>33</sup> 5.8% in Wolaita Zone, Sheferaw et al.,<sup>34</sup> 5.85% in three agro-ecological areas of Wolaita Zones, Kassaye and Kebede,<sup>35</sup> 8.11% in Tigray region, Seid et al.,<sup>36</sup> 7.5% in Eastern Amhara (Bati and Kombolcha) region, and Seyoum et al.,<sup>37</sup> 0.66% in Sekela, Amhara Regional State. However, It was lower than the report of Demissie et al.<sup>38</sup> 59.6% from Amhara regional state. The lower occurrence of mite infestation of goats in

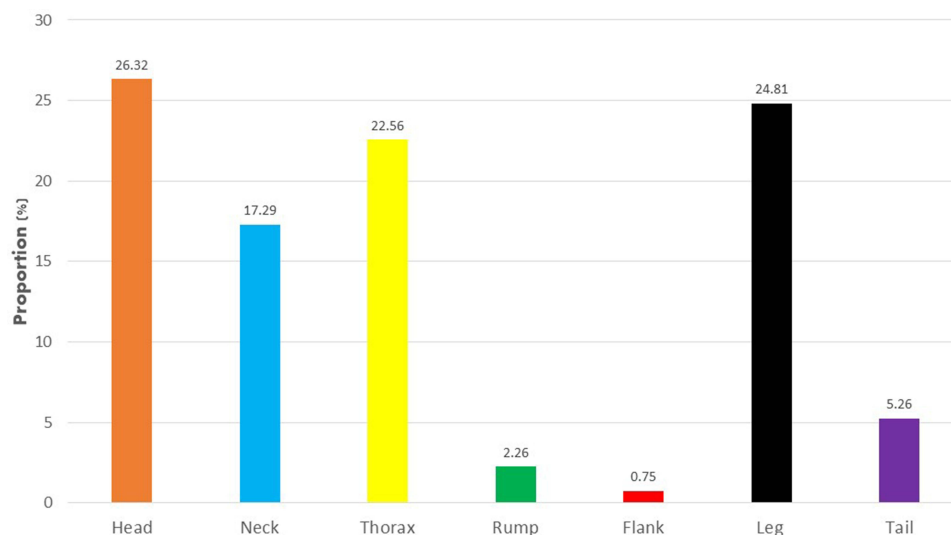
our study might be due to the implemented field-based control practice.

*Sarcoptes* were the predominant mite species identified in Malle district followed by *Psoroptes* and *Demodex* species. This was comparable with the finding of Numery<sup>39</sup> with a prevalence of 33.27% (*Sarcoptes*) and 1.36% (*Demodex*), and Tadesse et al.<sup>19</sup> with the prevalence of 30.3% (*Sarcoptes*) and 1.51% (*Demodex*) in goats of the Kombolcha Area. This is most likely due to the warmer temperatures, higher humidity, and more sunshine found in the midland and lowland agro-ecological areas, which are ideal for mite reproduction and multiplication.<sup>40</sup> The frequency of sarcoptic mange infection in the present study was higher than the previous report of Yasine et al.<sup>9</sup> of 10.3% in the Oromia zone of Amhara regional state. However, their finding of *Demodex* (2.8%) was comparable to our results. On the other hand, their finding of *Psoroptes* (0.6%) was much lower than our results.

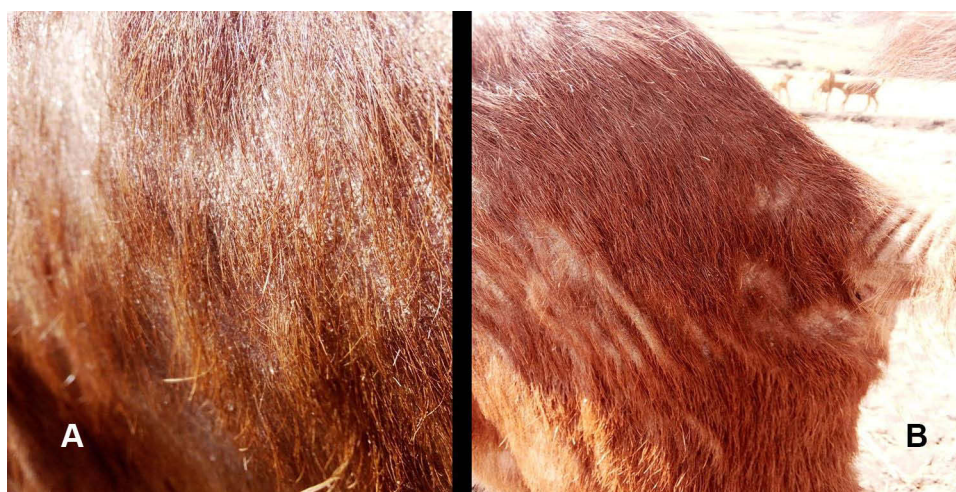
**Table 2** Prevalence of Mange Mites in Goats by the Different Factor Levels (N = 384)

Variables	Category	No. of Examined Animals	No of Positive Animals (%)	X <sup>2</sup>	p-value
Sex	Female	217	53 (39.8)	22.98	0.0001
	Male	167	80 (60.2)		
Age	Old	159	40 (30.1)	1.22	0.543
	Adult	109	50 (37.6)		
	Young	116	43 (32.3)		
Body condition scores	Good	83	23 (17.3)	2.41	0.29
	Moderate	147	52 (39.1)		
	Poor	154	58 (43.6)		





**Figure 2** Distribution of mange infection lesion in different parts of the body of goats.



**Figure 3** Gross lesion of mange mites infection in flank area (A) and leg and tail area of the goat (B).

Moreover, the previous reports of Mandado et al.,<sup>33</sup> 5.8% in the three agro-ecological districts of Wolaita Sodo, Sertse and Wossene,<sup>40</sup> 6.9% in Amhara regional state, Tadesse,<sup>41</sup> in the Dire Dawa Region, Nuru and Mhatebu,<sup>8</sup> in Haramaya districts, Molu<sup>42</sup> in the southern rangelands, and Haffize,<sup>43</sup> in central Ethiopia, Agegnehu et al.,<sup>44</sup> in Wag-Himra zone, Ethiopia, Asnake,<sup>45</sup> in selected districts of SNNPR, Kedir,<sup>46</sup> in Tigray, Teshome et al.,<sup>47</sup> with 4.3% in goats in the Sidama zone, Yacob et al.,<sup>48</sup> 0.98% in goats in Wolaita Sodo and Beyecha et al.,<sup>16</sup> 8.8% in goats in central Oromia were lower than our current study finding. The lower prevalence of mange infection might be partially due to the provision of an extensive ectoparasite control program in the study site

and this also might have created a good perception of the goat owners.

According to Soulsby<sup>49</sup> and Kambarage and Kusiluka,<sup>50</sup> age has a potential role in the incidence of different ectoparasitic diseases including mites. However, our study revealed that age has no role in the occurrence of mange infection in goats. Sheferaw et al.<sup>34</sup> in the Wolaita zone and Sertse and Wossene,<sup>40</sup> in the Eastern Amhara region reported that age is not a potential risk factor for the prevalence of mite infestation, which matches the current finding.

In the present research, mange infection was higher in male than female goats. Similarly, Seid et al.,<sup>36</sup> in the Eastern Amhara region also stated that males were more

**Table 3** Questionnaire Survey Output on Various Factors Related to Mange Mite Infestation on Goats in Male District (N = 153)

Variables	Category	No. of Respondents	Response (%)
Purpose of keeping goats	Source of income	128	83.66
	For home consumption (meat and milk)	25	16.33
Age group of infected goats	Old	58	37.91
	Adult	65	42.5
	Young	30	19.6
Season of mange mites infestation	Dry season	131	85.62
	Wet season	22	14.37
Ectoparasites causing skin disease	Mange mites	98	64.05
	Tick	38	24.83
	Lice	17	11.11
Method of treatment	Modern	132	86.27
	Traditional	21	13.72
Participation of farmers in the control practice	Yes	149	97.4
	No	4	2.61

infected with mange mites than females. This might be due to repeated contact between male and female goats during copulation and fighting that is mostly taken between male goats. Besides, sex hormones such as gonadal steroids may also contribute to immunosuppression that predisposes them to mite infection.<sup>51</sup> According to the current investigation, there was a significant correlation ( $p = 0.0001$ ) between sex and mange infection. This was against the previous report of Seid et al.,<sup>36</sup> in selected sites of the Eastern Amhara region, Sheferaw et al.<sup>34</sup> in three agro-ecological areas of the Wolaita zone, and Kassaye and Kebede<sup>35</sup> in the Tigray region, who reported sex has no significant effect on the occurrence of mange infection. Soulsby<sup>49</sup> also described that mange mite infestation occurs independently of sex.

Our results showed that mange infection severely affects poorly conditioned goats compared with goats in moderate and good condition. However, there was no significant correlation between the mange infection and the body condition of the goats. Similarly, the finding of Yasmine et al.,<sup>9</sup> Nuru and Mhatebu,<sup>8</sup> Kedir,<sup>46</sup> and Sertse and

Wossene<sup>40</sup> revealed that the risk of mange infection was 4.3 times higher in goats in poor condition than those in good condition. This finding might be due to poorly conditioned animals being more susceptible and unable to protect themselves from mange infection, which results in weight loss and productivity loss.<sup>40,52</sup> However, Seid et al.,<sup>36</sup> reported that goats in good condition were more infected with mange mite than poorly conditioned goats.

Radostits et al.<sup>53</sup> and Soulsby<sup>49</sup> reported that animals in good condition can resist parasite infection better than emaciated animals, which can influence the level of immunity. In line with this, the prevalence of mange mites was significantly higher in poor condition animals than in moderate and strong body condition animals. A similar result was reported by Sertse and Wossene,<sup>40</sup> and Kassaye and Kebede.<sup>35</sup>

The current research showed that mange mites were major ectoparasites of goats that affect all age groups, both sexes, and various body conditions. Mange infections had a great impact on the skin of ruminants. Similarly, Kassa et al.<sup>54</sup> stated that mites were among the major skin parasites that contribute to skin rejection in the tannery industry of Ethiopia. Akomas et al.<sup>55</sup> reported that mange mites were economically important ectoparasites of sheep and goats in Africa as well as in Ethiopia.

The current interview revealed that all the study participants rear their goats to generate money, home meat, and milk. Most respondents used modern therapeutic agents such as ivermectin 1% and acaricides to treat mange mite in goats whereas ethnomedicines were also used as a treatment by a few study participants of the area. This finding was consistent with the finding of Agegnehu et al.<sup>44</sup> in the Wag-Himra zone, who reported that farmers prefer to treat their goats using modern (ectoparasitic drugs) treatment than traditional therapy. This might be due to the provision of training by the government on the control methods of different ectoparasites and as per the assessment, the owners were aware and satisfied with the outcome of the modern therapy.

Moreover, most participants explained that mange mites were the main external parasites of skin in the three sites of the Malle district compared with ticks and lice. This was in line with the reports of Yasmine et al.<sup>9</sup> and Agegnehu et al.<sup>44</sup> who explained mange mites were the main ectoparasites affecting their sheeps and goats. The favorable climatic conditions of the areas have contributed to the survival and development of mites. The respondents also replied that adult goats were more susceptible to

mange infection than old and young age groups. The possible explanation for this might be due to various factors. Adult goats were kept outdoors so the chance of acquiring the different ectoparasites like mites were higher than younger ones that were kept indoors until they become stronger.

According to our findings, mite infestation was more commonly seen during the dry season compared with the wet season. This was in line with the finding of Seid et al.,<sup>36</sup> Yasine et al.<sup>9</sup> and Agegnehu et al.<sup>44</sup> The fact that mange mites are more common in goats during the dry season may be due to the goats' increased contact during shade-seeking from high-temperature stress<sup>56</sup> and also the existence of a higher goat population in the area.

Poor health care, starvation, and animal owners' lack of awareness about mange mites have all been proposed as contributing factors to this widespread infestation.<sup>9,15,16</sup> The findings of the questionnaire survey backed up these claims, as owners are normally only aware of the consequences of mites when the disease has progressed to the point that irreversible permanent harm has occurred. This finding corresponds to a previous study from the Amhara regional state.<sup>40</sup>

Most of the respondents in the area participated in the control program launched by the government. In addition to that, the respondents explained transmission of mange mite was mainly by direct skin contact between goats during bedding, grazing, and watering places. This might be due to the provision of a strategic control program.

## Conclusion

In this study, a high prevalence of mange mites was observed in the study sites. Factors such as sex, age, and body condition were found to be important in the occurrence of mange mite infection in goats. In conclusion, the veterinarians and concerned authorities should continue their activities of controlling these parasites through appropriate extension programs. It is known that the disease has a high economic impact especially on the skin of the animal. Farmers should be informed about the effect of mange and its economic significance. Besides, they also are advised to give more emphasis to pastorals, goats with poor body condition and adult goats to have a good prevention and control approach. Further epidemiological research on the economic and zoonotic significance of mites in various animal species, agro-ecological zones, and wildlife-domestic animal interactions is required.

## Data Sharing Statement

All the datasets generated or analyzed during this study were included in this manuscript.

## Ethical Consideration

The best practice guidelines for veterinary care were followed during sample collection and those goat owners were informed as to the purpose of the study, and that the Research Ethics and Review Committee approved this research work.

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## Author Contributions

All authors contributed significantly to the conception and design, data collection, and data review and interpretation; participated in the drafting of the article or critically revised it for relevant intellectual content; agreed to send to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of this work.

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## Disclosure

All authors declared no conflicts of interest for this work.

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