

The Impact of COVID-19 Crisis on Animal Service Deliveries in Central Areas of Ethiopia

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Abstract: A novel coronavirus outbreak is an infectious pandemic that is occurring in 2019. Instead of being SARS or influenza, it is a zoonotic virus that may spread to people. COVID-19 was emerged at the end of 2019 in China in Wuhan, the capital of Hubei China. The two most significant and well-known methods of virus transmission are direct physical contact and inhalation. The purpose of this study is to assess the status of COVID-19 in the local community and how it affects the provision of animal services in the Ethiopian regions of Adea Berga, Ejere, and Wolmera. All 132 respondents (18 female, 113 male), 49 (37.4%) from Adea Berga, 41 (31.3%) Ejere and 49 (31.3%) Wolmera have information about the introduction of the pandemic in Ethiopia via mass media (radio and television, 81.8%). Most respondents (49.2%) confirmed those old age groups were the most vulnerable age category. Animal health service deliveries were reduced by 9.9% in Adea Berga, 1.5% in Ejere and 5.3% in Wolmera after the introduction of COVID-19 in Ethiopia. The occurrences of animal diseases were increased by 13% in Adea Berga, 0.8% in Ejere and 4.6% in Wolmera due to this pandemic. Increasing the knowledge of population and secure supplies, inputs and services for small holder farmers, medium and large scale farm owners is mandatory in the area.

Keywords: Awareness, COVID-19, Service Delivery, West Shoa

1. Background

A broad family of viruses known as coronaviruses can infect either humans or animals and lead to disease. They (CoVs) are positive-sense, single-stranded RNA viruses that are enveloped [24]. There are now seven coronaviruses known to infect humans worldwide, although the four human coronaviruses 229E, NL63, OC43, and HKU1 are the most often transmitted [27]. They typically cause respiratory infections, particularly in humans, ranging from a minor cold to more serious illnesses like the Middle East Respiratory Syndrome (MERS) [1] and Severe Acute Respiratory Syndrome (SARS) [16], as well as the most recent coronavirus (COVID-19), which causes an infectious disease [1].

Coronavirus is currently one of the major infections that mostly affect the human respiratory system. The severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV, which have previously been defined as agents that pose a serious threat to public

health, are examples of earlier outbreaks of coronaviruses (CoVs) in various countries. A group of people were admitted to hospitals in late December 2019 with the initial diagnosis of pneumonia with an uncertain origin [10]. These individuals had an epidemiological connection to a wholesale market for seafood and wet animals in Wuhan, Hubei Province, China [1, 3, 23]. This infectious disease was once known as Novel Coronavirus-Infected Pneumonia (NCIP) by the WHO [11, 22], and the virus was known as 2019 Novel Coronavirus (2019-nCoV). On 11th Feb 2020, the WHO officially renamed the clinical condition COVID-19 (a shortening of Corona Virus Disease-19), which was announced in a tweet.

The virus is typically rapidly spread from one person to another via respiratory droplets produced during coughing and sneezing. It is considered most contagious when people are symptomatic, although transmission may be possible before symptoms show in patients. Time from exposure and

symptom onset is generally between two and 14 days, with an average of five days [8]. Common symptoms include fever, cough, sneezing and shortness of breath [4, 9, 15]. Complications may include pneumonia, throat pain and acute respiratory distress syndrome. Currently, there is no specific antiviral treatment or vaccine; efforts consist of symptom abolition supportive therapy. Recommended preventive measures include washing your hands with soap, covering the mouth when coughing, maintaining 1-meter distance from other people and monitoring, reliable and up-to-date information about the pandemic and self-isolation for fourteen days for people who suspect they are infected and using hand sanitizer [5]. The standard tool of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a throat swab or nasopharyngeal swab. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia [22].

Humans and some animals are both impacted by the zoonotic SARS-CoV-2 [19]. It is not surprising to find domestic animals exposed to the virus, either through environmental contamination or through human-animal contact, while residing close to COVID-19 positive human patients [19]. In the homes of COVID-19 patients, positive polymerase chain reaction (PCR) results have been recorded in domestic pets like dogs and cats [12]. Additionally, neutralizing antibodies were detected in certain cats' samples that were gathered following the outbreak in Wuhan, Hubei Province [18, 20, 26]. These preliminary findings raise the idea that domestic animals can contract the virus from people and the potential role that domestic animals may play in the spread of the virus among themselves. Similar potential reverse zoonotic transmission has been seen in other settings such as tigers in Bronx Zoo and minks in two farms in The Netherlands [21].

Understanding and addressing any challenges to food systems, agricultural production, and livelihoods requires an understanding of how people, animals, and the environment are interconnected. This is crucial in rural communities that raise livestock since animals are vital to society and food security because they provide clothing, transportation, fuel, revenue, and other necessities in addition to food. FAO embraces this issue and suggests a One Health strategy, where animal, human, and environmental health is all intertwined for the best outcomes.

Currently in Ethiopia COVID-19 is highly spreading among the people especially in and around the capital city Addis Ababa. There is high intensification between peoples in public transport, public market and Hotels especially in capital city and zonal city. Ministry of Health exhaustively diagnoses suspected groups, vulnerable peoples and medical practitioners, people who had contact with infected peoples and immigrants. Farmers and low income peoples did not have deep awareness about the pandemic. The effect of the condition on animal service delivery system and feed supply is very serious due to movement restriction and economical degradation within

the farmer. In order to ascertain the risk factors for infection and zoonotic transmission and to develop suitable strategies to reduce transmission between people [14], it is crucial to evaluate the disease's state, its impact on the provision of animal health services, and community knowledge. Therefore, the following goals were pursued in writing this paper:

1. To assess the status of COVID-19 pandemic in the area.
2. To assess the effect of COVID-19 on animal service delivery in the area.

2. Result

2.1. Socio-Demographic Characteristics of the Respondents

A total of 131 respondents (113 men and 18 women) were interviewed to assess the status of COVID-19 in the local area and how it affected the provision of animal services. 49 (37.4%) of those who responded were from Adea Berga, 41 (31.3%) were from Ejere, and 41 (31.3%) were from the Wolmera region. 74% of people who responded to the survey fell within the 31–60 age range. According to respondents' educational backgrounds, 35.9% can read and write, 19.1% cannot, and nearly half were in grades primary and above. In addition, 106 (80.9%) of the participants were married, and 11 (8.4%) were not.

Table 1. Socio-economic characteristics of respondent.

Variables	Number of respondents	Percentage (%)
Study site		
Adea Berga	49	37.4
Ejere	41	31.3
Wolmera	41	31.3
Sex		
Female	18	13.7
Male	113	86.3
Age category		
Young (<30years)	19	11.5
Adult (31-60years)	97	74
Old (>60years)	15	14.5
Marital status		
Married	106	80.9
Unmarried	11	8.4
Divorced	14	10.7
Educational status		
Unable to read and write	25	19.1
Read and write	47	35.9
Primary and above	59	45
Main source of income		
Trade	2	1.5
Gov't/private employment	16	12.1
Agriculture	102	77.3
Trade and agriculture	2	1.5
Employment and agriculture	9	6.8

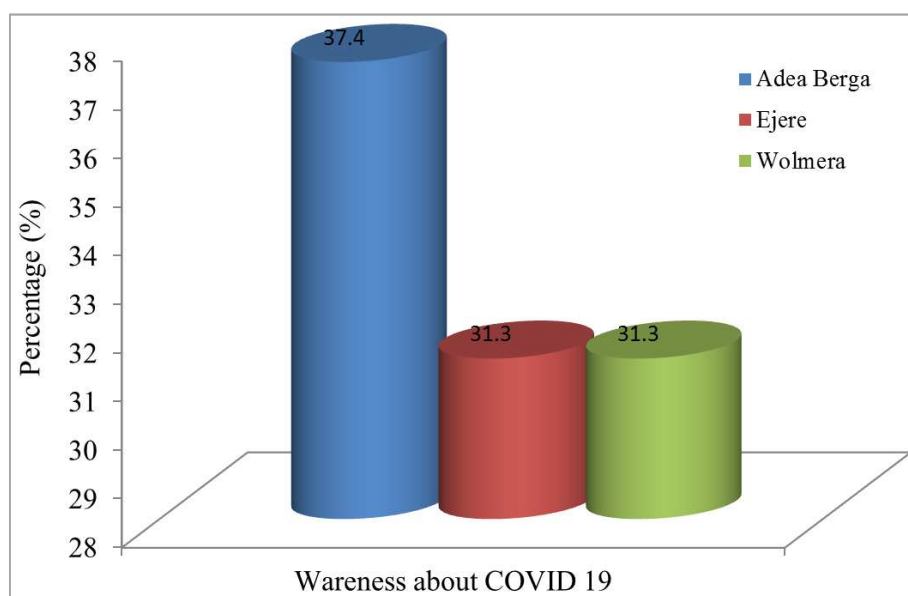
In Adea Berga district 19.5% dairy cattle owned were cross breed dairy cows. In the other hand in Ejere district 33.6% of livestock were oxen.

Table 2. Livestock ownership status of respondents.

Livestock	Addea Berga	Ejere	Wolmera
	No. of animal (%)	No. of animal (%)	No. of animal (%)
Dairy cow			
Local	121 (27.1)	59 (13.2)	70 (15.7)
Cross	87 (19.5)	45 (10.1)	66 (14.8)
Total	208 (46.6)	104 (23.3)	136 (30.4)
Heifer			
Local	41 (27)	25 (16.4)	21 (13.8)
Cross	19 (12.5)	21 (13.8)	25 (16.4)
Total	60 (39.5)	46 (30.3)	46 (30.3)
Calf			
Local	37 (24.7)	30 (20)	22 (14.7)
Cross	27 (18)	14 (9.3)	20 (13.3)
Total	64 (42.7)	44 (29.3)	42 (28)
Oxen			
Local	62 (24.5)	85 (33.6)	53 (20.9)
Cross	27 (10.7)	12 (4.7)	14 (5.5)
Total	89 (35.2)	97 (38.3)	67 (26.5)
Poultry			
Local	76 (14.8)	96 (18.6)	72 (14)
Cross	86 (16.7)	99 (19.2)	86 (16.7)
Total	162 (31.5)	195 (37.9)	158 (30.7)
Sheep and goat	111 (43.5)	53 (20.8)	91 (35.7)

2.2. Assessment of COVID-19 Status in the Community

According to the survey result; currently all respondents in both three woreda have information about COVID-19 pandemics in Ethiopia.

*Figure 1. Respondents awarenss about COVID-19.*

Most respondents in each kebeles (27.5%) got information about COVID-19 were through mass medias like radio and television. Out of 131 interviewed respondents from three woredas a total of 6 respondents were trained, 2 (1.5%) from Adea Berga, 1 (0.8%) from Ejere and 3 (2.5%) from Wolmera. In Ejere woreda 1 (0.8) and Wolmera 2 (1.5%) individuals were infected with COVID-19 during the study time.

Table 3. Assessment of COVID-19 status within the population.

Variables	Adea Berga	Ejere	Wolmera	X ² - value	P-value
	No. of respondents (%)	No. of respondents (%)	No. of respondents (%)		
Source of information					
Mass media	36 (27.5)	36 (27.5)	36 (27.5)	16.551	0.005

Variables	Adea Berga	Ejere	Wolmera	X ² - value	P-value
	No. of respondents (%)	No. of respondents (%)	No. of respondents (%)		
Health extension	0	0	1 (0.8)	2.38	0.293
Family and friends	2 (1.5)	2 (1.5)	3 (2.3)		
More than one source	11 (8.4)	2 (1.5)	0		
Positive report in community				1.161	0.674
Yes	0	1 (0.8)	2 (1.5)		
No	49 (37.4)	40 (30.5)	39 (29.8)		
Training about the disease				1.161	0.674
Yes	2 (1.5)	1 (0.8)	3 (2.5)		
No	42 (35.9)	40 (30.5)	38 (29)		

2.3. Association of Factors with COVID-19 Status in the Area

Univariable Logistic Regression analysis was computed to evaluate the association between COVID-19 status and different risk factors. Out of 131 interviewed respondents, 4

(3.1%), 2 (1.5%) and 3 (2.3%) from Adea Berga, Ejere and Wolmera were tested for COVID-19. None of them are positive for the test. The analysis indicates that there was no statistically significant association between COVID-19 status and different factors ($P > 0.05$) (Table 4).

Table 4. Univariable Logistic Regression analysis of factors related to COVID-19.

Variables	Tested for COVID-19 (%)	Untested for COVID-19 (%)	OR (95%CI)	P-value
Location				
Adea Berga	4 (3.1)	45 (34.5)	1	1
Ejere	2 (1.5)	39 (29.8)	0.966 (0.9415-1.2931)	0.222
Wolmera	3 (2.3)	38 (29)	0.977 (0.8666- 1.0781)	0.539
Age				
Adult	7 (5.3)	90 (68.7)	1	1
Young	0	19 (14.5)	0.94 (0.823-1.06759)	0.326
Old	2 (1.5)	13 (9.9)	1.04 (0.8942-1.9916)	0.639
Sex				
Female	2 (1.5)	16 (12.2)	1	1
Male	7 (5.3)	106 (80.9)	0.96 (0.8354-1.1005)	0.547
Educational status				
Primary and above	2 (1.5)	57 (43.5)	1	1
Read and write	4 (3.1)	43 (32.8)	1.05 (0.9447-1.1581)	0.384
Unable to read and write	3 (2.3)	22 (16.8)	1.07 (0.9432-1.2209)	0.281

According to respondents response old age groups were the most vulnerable age category. About 28 (21.4%), 17 (13%) and 20 (15.3%) of respondents from Adea Berga, Ejere and Wolmera districts were confirmed that old age humans were most affected group by COVID-19 respectively.

Table 5. Most affected age group.

Most affected age group	Adea Berga	Ejere	Wolmera	X ² -value	P-value
	No. of respondent (%)	No. of respondent (%)	No. of respondent (%)		
Old age	28 (21.4)	17 (13)	20 (15.3)	2.212	0.3309
Adults	1 (0.8)	4 (3.1)	1 (0.8)	3.666	0.1599
Youngster	2 (1.5)	1 (0.8)	1 (0.8)	0.279	0.8695
Children	1 (0.8)	1 (0.8)	0	0.9487	0.6223
All ages	7 (5.3)	11 (8.4)	10 (7.6)	2.413	0.2992
Co-infected with other disease	2 (1.5)	1 (0.8)	0	1.667	0.4343
Old and co-infected patient	2 (1.5)	0	2 (1.5)	1.927	0.3815
Old and children	4 (3.1)	3 (2.3)	6 (4.6)	1.499	0.4725
No idea	2 (1.5)	3 (2.3)	1 (0.8)	1.1607	0.5597

2.4. Effect of COVID-19 on Animal Service Delivery

Restrictions on movement during efforts to contain the COVID-19 pandemic are affecting the livelihoods of livestock-owning households through reduced access to animal health care, inputs, markets, and even to pastures and water. Animal health and other related service did not totally terminated due to the pandemic. Only 9 (6.9%), 1 (0.8%) and

1 (0.8%) respondents from Adea Berga, Ejere and Wolmera respectively reported that there is no animal health extension service. On the other hand it causes the decline of health and other related service in the study areas. Veterinary drug and supply was also reduced when compared to pre COVID-19 pandemic in both areas of assessment. Reduction in service and increase in farm impute cost caused by the pandemic results animal disease outbreak and death in the study area.

Table 6. Effect of COVID-19 on animal service delivery.

Effect of COVID-19 on service delivery	Adea Berga No. of respondent (%)	Ejere No. of respondent (%)	Wolmera No. of respondent (%)	X ² -value	P-value
Extension service					
Yes	40 (30.5)	40 (30.5)	40 (30.5)	10117	0.006**
No	9 (6.9)	1 (0.8)	1 (0.8)		
Service due to COVID-19					
Decrease	13 (9.9)	2 (1.5)	7 (5.3)	7.493	0.021*
Remain the same	36 (27.5)	39 (29.8)	34 (26)		
Shortage of veterinary drug and vaccine					
Yes	9 (6.9)	7 (5.3)	10 (7.6)	1.197	0.889
No	29 (22.1)	24 (18.3)	24 (18.3)		
No idea	11 (8.4)	10 (7.6)	7 (5.3)		
Disease outbreak					
Yes	12 (9.9)	1 (0.8)	1 (0.8)	11.458	0.004**
No	37 (28.2)	40 (30.5)	38 (29.2)		
Disease occurrence					
Increase	17 (13)	1 (0.8)	6 (4.6)	16.061	0.000***
Remain the same	23 (24.5)	40 (30.5)	35 (26.7)		
Death occurrence					
Yes	11 (8.4)	3 (2.3)	3 (2.3)	6.219	0.051***
No	38 (29)	38 (29)	39 (29)		

COVID-19 pandemic in the study areas causes reduction in revenue, lack of market, lack of work force, lack of transport to purchase farm impute, lack of transport to sell farm output and increase of farm impute price.

Table 7. Impact of COVID-19 on farm imputes and output.

Variables	Adea Berga Respondents (%)	Ejere Respondents (%)	Wolmera Respondents (%)	X ² -value	P-value
Decrease revenue					
Yes	18 (13.7)	7 (5.3)	19 (14.5)	8.22	0.017
No	31 (23.7)	34 (26)	22 (16.8)		
Lack of market					
Yes	19 (14.5)	8 (6.1)	15 (11.5)	4.364	0.123
No	30 (22.9)	33 (25.2)	26 (19.8)		
Lack of work force					
Yes	5 (3.8)	0	7 (5.3)	7.284	0.031
No	44 (33.6)	41 (3.3)	34 (26)		
Lack of transport to purchase farm impute					
Yes	20 (15.3)	11 (8.4)	19 (14.5)	3.54	0.17
No	29 (22.1)	30 (22.9)	22 (16.8)		
Lack of transport to sell farm output					
Yes	19 (14.5)	10 (7.6)	14 (10.7)	2.142	0.368
No	30 (22.9)	31 (23.7)	27 (20.5)		
Increase of farm impute price					
Yes	39 (29.8)	31 (23.7)	38 (28.2)	4.917	0.312
No	10 (7.6)	9 (6.9)	3 (2.3)		
No idea	0	1 (0.8)	1 (0.8)		

3. Discussion

The pathogenic agent that causes COVID-19 is known as SARS-Coronavirus-2 (SARS-CoV-2) and was first discovered in December 2019 [13]. SARS-CoV-2 is believed to have originated from an animal source before spreading to people [17]. Although genetically similar viruses have been discovered from Rhinolophus bats, it is still unknown where SARS-CoV-2 originated from and how it entered the human population. SARS-CoV-2 is mostly spread from person to person through respiratory droplets that infected individuals may sneeze, cough, or exhale [4]. Even though the genetic sequences and other data that are currently available indicate

that the SARS-CoV-2 virus originated from an animal source, there is currently insufficient information to pinpoint the exact source or the path of transmission from the initial animal reservoir to a possible intermediate host and then to humans. Studies are being conducted to evaluate the dynamics of infection in sensitive animal species and to better understand the vulnerability of various animal species to SARS-CoV-2 [3].

The alarming spread of COVID-19 is currently a significant global public health concern. There is currently no known cure or vaccine for it. Therefore, the best course of action is prevention. By improving the populations' knowledge, attitudes, and practices about COVID-19, especially in high-risk groups, COVID-19 can be prevented

and controlled effectively. The current investigation found that every respondent was aware of COVID-19's introduction and the disease's incidence in the study area. Currently, COVID-19 is a hot topic in the media and among the general population [2].

The main source of information in this study was TV and/or radio (27.5% Adea Berga, Ejere and Wolmera each while that of the study by [2] was social media (60%). This difference might be due to a difference in study populations' socioeconomic and educational status.

Movement restrictions and disruption of national and international trade routes is curbing farmer access to animal health extension service. In Adea Berga 6.9% of respondents, Ejere 0.8% and Wolmera 0.8% respectively confirmed that animal health extension service was terminated due to the impact of COVID-19. The lower impact in Ejere and Wolmera may be due to the urbaneness of the area. In urban area private animal health clinic may give service.

According to our finding, 29.8% of respondents from Adea Berga, 23.7% from Ejere and 28.2% from Wolmera reported that price of farm imputes (especially feed) was increased after COVID-19 pandemic. This could be the result of forced closures of non-essential businesses, travel restrictions, and border controls that prevent farmers from gaining access to farming inputs, supplies, and equipment like feed, replacement stocks (chicks, piglets, gilts), breeding materials, and milking machines; cause a brief labor shortage; and lead to animal and animal product loss or waste. The effectiveness of industrial feed businesses is also being hampered by physical separation and the need for additional personal safety equipment. Labor shortages and a decline in the supply of raw materials or other ingredients are the results of movement limitations and illness. Feed delivery has been further delayed by the disruption of supply channels.

During COVID-19 pandemic animal disease outbreaks were encountered in the area. 9.9% of respondents reported animal disease outbreak. The may be caused by the disruption of public services (like animal health extension services), combined with interrupted delivery and use of vaccines and medicines due to COVID-19 that can increasing the likelihood of new epidemics. Animal diseases also cause livestock losses in the area.

4. Conclusion and Recommendations

An infectious disease known as Novel Coronavirus Disease 2019 (COVID-19) is caused by a coronavirus 2 that causes severe acute respiratory syndrome (SARS-CoV-2). In terms of deaths and financial costs, COVID-19 is an unintentional worldwide health burden, particularly for developing countries like Ethiopia. People's awareness in the study regions is raised through frequent advertising in the media that includes facts about the frequency of common diseases as well as advice papers (simple control methods). Due to the transportation restrictions, there is less ability to work on activities related to animal health, such as vaccinations, medical care for sick animals, and preventative

treatment for local specialists. Animal welfare requirements may be compromised by overcrowding on farms, which could raise stress and the prevalence of animal diseases. Reduced production performance may result from this. Farmers' access to fundamental veterinary services is limited by prohibitions on movement and quarantine measures. Farmers' access to animal health and nutritional inputs, such as veterinary medicine, vaccines, disinfectants, and feed supplies, is impacted by the impact on logistics and supply chains.

The following suggestions are made in light of these findings:

1. Stay current with trustworthy information and educate farmers on necessary behavioral adjustments.
2. Ensure that small-scale, medium-scale, and large-scale farmers have access to supplies, inputs, and services.
3. Follow the WHO-recommended personal biosafety and biosecurity precautions as well as general hygiene guidelines for COVID-19.
4. The Woreda Agricultural Bureau is required to have a stock of medications, drugs, antiseptics, personal protective equipment, diagnostic tests, supplies, and equipment.

5. Material and Methods

5.1. Study Area

The study was conducted in the major milk sheds of Addis Ababa; Wolmera, Adea Berga, and Ejere districts, in the Oromia regional state of Ethiopia, are noted for their highly developed dairy output.

The Wolmera District is located in the Oromia Special Zone that surrounds Addis Ababa. It is situated 29 kilometers west of Addis Ababa at 9° 30' N and 38° 30' E, between 2300 and 3800 meters above sea level, and is truly a portion of Ethiopia's central highlands. The yearly high and low temperatures were 6 and 22 degrees Celsius, respectively. In addition, the region is occasionally frosty from October to December, when temperatures occasionally dip below zero for a few days. Rainfall varies between 900 to 1100 mm every year. The area's main livestock production systems include market-driven, peri-urban dairy production and urban dairy production systems. Mixed crop-livestock farming around the towns, where animals are kept under extensive traditional grazing systems [7]. The projected total number of cattle is 175,741, of which 172,769 (98.3%) are local breeds and 2972 (1.7%) are crossbred cattle raised under extensive and semi-intensive management systems [25].

Adda Berga is one of the woredas in Ethiopia's Oromia Region, and it is situated at 9° 15' 0" N and 38° 25' 0" E. This woreda had a total population of 120,654 according to the 2007 national census, 60,366 males and 60,288 women; 3.21% of its population, lived in cities [6].

One of the woredas in Ethiopia's Oromia Region is Ejere, which is located at 8° 55' N 38° 35' E. It is a part of the West Shewa Zone and is bounded by the Southwest Shewa Zone on the south, Dendi on the west, Jeldu on the northwest, Meta

Robi on the north, Adda Berga on the northeast, and Walmara on the east. This woreda had a total population of 86,934 according to the 2007 national census, of which 44,222 males and 42,712 women made up the population. 11.59% of the total lived in cities [6].

5.2. Study Population

Dairy cow owners in the districts of Adea Berga, Wolmera, and Ejere were the study's target populations. Employees from the public and private sectors, farmers, and business owners who deal directly with dairy cows and are willing to sign an informed consent form when they are at least 18 years old were all included in the study.

5.3. Study Design

From August 2020 to October 2020, a cross-sectional study was done to assess the status of COVID-19 in the community and how it affected the provision of animal services.

5.4. Sampling Technique and Sample Size Determination

Purposive sampling technique was applied to select three districts from west Shoa zone. Three districts; Wolmera, Adea Berga and Ejere, were selected from west Shoa based on accessibility and livestock density. Each household and respondents were selected randomly. Accordingly 49 respondents from Adea Berga, 41 from Wolmera and 41 from Ejere Districts were interviewed structured questioner.

Using the formula provided by Thrusfield (2007), the sample size for the study was determined. It had a defined precision of 5%, a 95% level of confidence interval, and an expected occurrence of 50%.

$$n = \frac{1.96^2 \times P_{ex} \times (1 - P_{ex})}{d^2}$$

Where, n=required sample size, P_{ex}=expected prevalence, and d=desired absolute precision.

Hence, based on the above formula and taking into account 50% prevalence, the minimum sample size is:

$$n = \frac{1.96^2 \times 0.5 \times (1 - 0.05)}{0.05^2}$$

$$n = 380$$

However, due to the current condition we cannot address the required amount of respondents. Therefore, a total of 131 respondents who have livestock were selected.

5.5. Data Management and Analysis

Data gathered from the field was coded, saved in an Excel spreadsheet created with Microsoft Office, and then transferred to R software version 4.0 for statistical analysis. Results from a descriptive questioner were analyzed using the Chi-square (χ^2) statistic.

Data Availability

The data used to support the findings of this study are

available from the corresponding author upon request.

Conflict of Interest

The authors declare that no conflict of interest between them.

Authors' Contributions

All author contributed to the conception of the research idea, designing and data collection. The first was conducting data analysis, interpretation of data, and writing and editing of the manuscript. All authors read and approved the final manuscript.

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