Reproductive problems in small ruminants (Sheep and goats): a substantial economic loss in the world

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SUMMARY

The primary fortitude of this study is to overview the environmental, nutritional and also some main infectious causes related to reproduction in small ruminants mainly sheep and goat, that caused milk, meat and wool production loss globally. Mostly 90% small ruminants are reared by rural household globally. The major issues of which are poverty, lack of new techniques and improper management skills. Families usually own few small ruminants, which are used for religious celebrations, serve as savings or emergency cash or provide meat or milk. Reproductive problems mainly arise due to nutritional deficiencies and some pathogens, including bacteria, viruses, parasites and also by environmental stress conditions. The primary reproductive diseases which are commonly associated with the reproductive system of small ruminants are brucellosis, leptospirosis, toxoplasmosis fever, listeriosis, campylobacteriosis along with nutritional deficiencies, socio-sexual and photoperiods also affect the reproductive system. Vaccination and nutrition are mainly advised to control these issues of reproduction. The environment control system can also compensate for this economic loss. This paper represents a limited contribution for the review of reproductive problems in small ruminants' primarily focusing on sheep and goat which was neglected in past at worldwide level.

KEY WORDS

Reproductive issues, nutritional deficiencies, photoperiods, socio-sexual effect, pathogen.

INTRODUCTION

Small ruminants (sheep and goats) play an important role in the survival, economic, and social livelihoods of many humans, more significantly in developing countries[1]. According to FAO (2010), roughly 95.7% of all goats and 63.3% of all ewes are located in developing countries and embody more than 70% of total animal production in the world[2]. Agreeing to the Food and Agriculture Organization (FAO), in 2011, there were 875.5 million goats and one billion sheep in the world. However, around 80% of all small ruminants were in developing countries, many of them placed in tropical areas. So, signifying more than 70% of their production of these species in developing countries (FAOSTAT 2011)[3]. Several diseases which affect the small ruminants mostly causing abortion, delayed estrous and reduced fertility. The diseases which cause abortion are campylobacteriosis and enzootic abortion. Toxoplasmosis, contamination caused by a *Toxoplasma (T.) gondii* apicomplexan protozoan, is common in humans an animal species, having already been testified in many countries and different weathers. Goats had significantly higher ($p<0.01$) prevalence (25.4%) as compared to that of sheep (11.2%); and higher ($p<0.01$) in female (24%) than in the males (19%) for both species[4]. Despite the status of small ruminants breeding in developing countries, milk/meat productivity remains insufficient. Communicable diseases such as leptospirosis, brucellosis, and small ruminant lentiviruses (SRLVs), add to this scenario[2]. Developing countries, due to the social, soil, and weather features, present a suitable scenario for development and increase of goats and sheep breeding. In the last decades, although the high number of small ruminant population in developing countries, its yield remains lower than that in developed ones[3].

Infectious diseases, particularly those of the reproductive domain, play a dramatic role in this scenario, causal important economic threats in livestock[5]. But it may vary according to management and related areal climate changes. Animals have developed reproductive strategies for enough food coincides with pregnancy and lactation. The economic and public health effect of brucellosis remained of a concern in developing countries. The diseases that generally cause a significant loss of productivity through abortion, stillbirth, low herd infertility and comparatively low milk production[6]. Under the name "Malta fever," the disease now called brucellosis first came to the attention of British medical officers in the 1850s in Malta during the Crimean War. Brucellosis is a zoonotic disease that leads to considerable illness. Also, it was characterized by abortion in females and epididymitis and orchitis in males[7].

The economic and public health effect of brucellosis remained serious concern in developing countries[8]. In general brucellosis can cause significant loss of productivity through abortion, stillbirth, low herd fertility and comparatively low milk production. It is thought that this can be achieved by linking sexual activity to changes in the photoperiod, a reliable predictor of the seasons and future food supplies, however, this is not applicable due to 3 reasons[1] photoperiods can change in, the region that, are close to the equator[2]. In many

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regions, the fodder availability can be determined by many factors other than photoperiods[3]. In semi-arid regions, the pattern of food supply mainly changes year to year due to unpredictable rain falls. However, low mineral intake or availability to small ruminant's results to reduce productivity. Natural grazing is also a source of obtaining minerals from forage plants. Thus, feeding places and seasons also affect the mineral status. Families commonly own a few small ruminants, which are used for religious festivities, serve as savings or spare cash or provide meat or milk. Consequently, due to the reduction of reproductive performance of the herd, whole milk, as well as meat production, tends to decrease, demonstrating an important hazard to farmers. The acceptance of adequate programs to reduce the incidence of infectious diseases[2]. Inadequate management practices and poor propagative performance have been reported as vital factors in decreasing productivity level in livestock. Diverse pathogens have been reported in small ruminants' herds/groups with reproductive failures. Subclinical infection is mainly categorized by reproductive problems, such as infertility, abortion, occurrence of stillbirths, and weak lambs/goat kids[3]. Reproductive problems caused by nutritional deficiencies and infectious diseases and other environmental stresses are mentioned here.

ENVIRONMENTAL CAUSES (PHOTO-PERIOD, SOCIO-SEXUAL)

Mostly reproductive response to environmental factors are coordinated at brain level, where all external and internal inputs ultimately converge into a final common pathway that controls secretion of gonadotropin-releasing hormone. This neurohormone controls the secretion of gonadotropins pituitary hormones that determined activity of reproductive axis[9]. The mechanism of feed flush has been done in sheep management for many years to increase breeding duration[10]. Thermal stress decreases the intensity of sexual behavior and also cause in failure of the animal to maintain a pregnancy and mating[11]. Sometimes heat effect causes a reduction in fetal growth[12]. If stress is imposed in the follicular phase of sheep, it causes to decrease in estrogen level concentration and also effect on late preovulatory GnRH/LH surge[13]. When ewes are under or above the critical temperature, their oestrus duration is delayed that is due to thermal stress[14] or when these are transported then due to transport stress[10].

For proper reproductive efficiency follicle must grow at proper rate in ovaries, ovulation should occur and related hormones that need to be produced not to control releasing but also to make uterus ready for conception. All these events are controlled by endocrine coordination which can be disturbed in stressed conditions[15]. The activities of the neurons are coordinated and synchronized so GnRH is released as a stream of pulses, the frequency of which is critical: a high frequency promotes the gonadal activity and a low frequency permits gonadal activity to minimize. Every pulse of GnRH releases a pulse as of gonadotropins luteinizing hormones from the pituitary glands in the males each LH pulse stimulates the ledying cells in the testes to release a pulse of testosterone which completes the loop by exerting "negative feedback k" on the hypothalamus system to minimize the frequency of GnRH and LH pulses[16]. The timing events in the reproductive process using male effect in sheep and goats, the sudden introduction of new males can induce ovulation in females that are reproductively quiet[16]. The male effect also work for advancing the 1st cycle in young females. Among the environmental factor affecting the reproductive system in sheep and goat the level and type of nutrition is also the most important factor which has also impact on reproduction[17].

EFFECT OF NUTRITION ON THE REPRODUCTION IN SMALL RUMINANTS

Limited feeding resources may cause a decrease in reproductive performance according to the required limit and reproductive status[18]. High feed intake can increases the reproductive output. While for short and long term under-nutrition may exert a negative effect on ovarian activity in goats[19]. The feed flushing system has been incorporated into the sheep and goat management system to increase the seasonal breeding period[15]. The interaction between nutrition and reproduction having a major role in sheep reproductive performance[17]. The relationship between ovary functioning and nutrition is a fundamental rule to maximize reproductive efficiency[20]. Deficient nutrition having long term effect on reproductive capabilities as pregnant ewes fed 50% of its requirement after mating from 28 to 78 days resulted offspring having lower stress response at one year of age, it also cause to lessen progesterone level in the luteal phase and also reduction in fertility when compared to control ewes[21]. Feed restriction is causing a decrease in GnRH amplitude, pulse and the capability of low amplitude GnRH pulses to generate a consequence LH pulse in ovariectomized ewes[10]. The magnitude of LH and FSH surge in pre-ovulatory stage may be diminished in fasting in ewes[18]. FSH and LH level tend to be decreased in fasted ewes[22]. Fasting decrease plasma concentration and FSH pulse amplitude in comparison to that of control significantly[23]. Short-term fed on high protein and energy diet causes an increase in blood glucose and insulin concentration in cyclic ewes and also affect the follicular environment particularly follicular fluid glucose level. The follicular fluid concentration of progesterone was negatively correlated with the follicular fluid concentration of glucose[17]. Fasting effects pituitary-hypothalamus ovarian axis that can be stimulated by metabolic meditators like glucose, insulin, GH, IGF-1 and IGFBP.

Nutritional effect on reproductive performance may be inter-linked via changes in the IGF-1 mechanism (IGF-1 and IGFBP) which is secreted by the liver and may be present in other reproductive tissues[24]. An acute nutrition restriction till the IGF-1 level decrease then it may cause a reduction in FSH-receptor expression by developing follicle to respond FSH[18]. Insulin and glucose are necessary as a source of nutritional folliculogenesis stimulation[17]. Progesterone synthesis and its release by ovary are also regulated pituitary gonadotrophin as well as by IGF-1 which is an important factor for ovarian secretory and granulosa cell proliferation activity. Glycaemia and insulinemia having a role in the regulation of ovarian follicles responsive to gonadotropin[25]. The insulin-dependent glucose transporter is also present in theca and granulosa cells of follicles in sheep. Insulin is also affecting granulosa and theca cell function. An increase in in-

sulin-mediated glucose is critical when up taken by follicle cells for growth and protection from atresia thus increasing ovulatory follicles in numbers. On the other hand, ovulation rate can also be affected by nutrition[22]. Fasting reduced the ovulation rate significantly in ewes[23]. Increasing dietary intake may affect the stimulation of follicular development and increases the ovulation rate in sheep. Acute feed restriction in the luteal phase of the estrous cycle in ewes cause the changes in endocrine functions that may affect the timing of LH surge and ovulation rate also[18]. Short-term fed on high energy and protein may cause changes in feedback mechanism between FSH and Estradiol[17]. Energy-deficient feed may cause lipid to break down which result into an increased level of non-esterified fatty acids and beta-hydroxybutyric acid including low glucose concentration in serum[27]. The resulted metabolites affect the endocrine signaling pathway and also affect the quality and number of oocytes[28]. Increased plasma non-esterified fatty acid level as a sign of negative energy balance that is linked to decreasing in fertility in goats[19]. Circulating urea and non-esterified fatty acids affect the quality of granulosa cells and also oocytes[27].

While short-term fasting may decrease the follicular growth, high plasma progesterone level and lowers the magnitude of LH and FSH surge in sheep[18]. Fasting causing a decrease in average plasma FSH level compared to the control group significantly[23]. The short term dietary treatments lead to changes in blood concentrations of glucose, fatty acids, insulins and leptins as well as the cerebrospinal fluid concentration of glucose, insulin, leptins and some amino acids. Some crucial factors seen to be fatty acids, insulin and leptin, all of which can maximize GnRH pulse frequency. Current studies showed that there are neuroanatomical connections between the centers that control the reproduction[9]. The acute fasting is having a negative effect on ovulation rate in ewes. It also causes a decrease in the level of LH, FSH, Leptin and changes in the signaling pathway of GH[23]. The increase leptin concentration is having an effect on LH secretion from pituitary cells within physiological range in-vitro. The synthesis of steroid hormones depends on the availability of cholesterol metabolites to ovarian theca and granulosa cells[29]. Intracellular cholesterol is transported by steroidogenic acute regulatory protein (**STAR**) from the outer mitochondrial membrane to the inner mitochondrial membrane[30]. Circulating urea has been negatively associated with fertility[31]. Dangerous effects on reproduction are stimulated by the direct effect of urea on the nuclear and cytoplasmic development of the follicle having oocyte[32].

INFECTIOUS CAUSES

Toxoplasmosis

Toxoplasmosis is a parasitic disease causing reproductive problems and enormous economic loss to the sheep industry all over the world[33]. Toxoplasmosis is an infection caused by *T. gondii* blood protozoan that is widespread in animal species reported many countries and many different climate conditions. Goats are having high prevalence than sheep and highly significant incidence in females than males[34]. The considerable incidence has also been noted in males than females[35]. Toxoplasmosis is protozoal a parasitic blood disease that causes severe reproductive issues and economic losses to the small ruminants all over the world[33]. *Toxoplasma gondii* has been recognized as an essential cause of lambing loss and food hazards (Innes et al., 2010). Prevalence of toxoplasmosis is varied from country to country and from climate to climate changes within a state[37].

The worldwide seroprevalence of toxoplasmosis in sheep is 30% while in goats 15%[38]. Age of animal is also a determining factor for the prevalence of toxoplasmosis in animals. Incidence is highest (38.88%) in the age group of 16-28 months and lowest (8.51%) in the age, group of 68-80 months and *T. gondii* is higher in younger animals than adults and body weight of the animal is also a key factor for prevalence[38]. *Toxoplasma gondii* is common in sheep's and goat's one of the significant causes of abortion in many countries. It can also affect fetus of pregnant females (AH/sheep/19). Within livestock sheep and goats are more easily infected with *Toxoplasma gondii* although infection has also been reported in cattle. Moreover, goats infected by *T. gondii* also represent a vital source of human disease due to ingestion meat and milk from infected animals[39]. It may cause resorption or mummified fetus if infected late in gestation may cause abortion or death soon after birth. Female are immune after abortion (AH/sheep/19). Cats are a primary reservoir and definite host, usually spread it only for few weeks as a kitten. Cats and rodent shed agent into hay and feed by their feces which are later ingested by sheep and goats. The disease is transmitted by ingestion of contaminated feed having oocytes and cyst of *Toxoplasma gondii*[38]. Uncooked meat and milk having cysts and oocytes may spread the disease to human by eating such food. Some studies show that sheep and goats are significant sources of infection in a human by eating uncooked meat and milk that cause a massive loss for a small ruminant breeder in many countries.

T. gondii has also been found in mutton and beef in many developed countries[40]. Keep cats away from feed storage and feeding areas. Some producer it best to maintain one adult cat which keeps younger cats away from the field. Burn aborted products[41]. Wear rubber gloves when handling with aborted fluid and tissues. It is one of the leading cause of abortion in many countries. Infection during early gestation may cause of reabsorbing of the fetus while in later stages abortions are most common. The abortion manner and disease are different from the bacterial cause of abortion.

Preventive Measures - Keep dog and cat away from feed storage and feeding areas. Some producers have found it best to maintain one adult, neutered cat which then tends to keep younger, stray cats away from the area. Because cats are reservoir of infecting agent.

Leptospirosis

Leptospirosis is a global zoonotic disease caused by pathogenic spirochetes *Leptospira interrogans* that belongs to genus Leptospira. Genus Leptospira consists of pathogenic and non-pathogenic according to DNA related species[42]. Leptospira colonies in the kidney in various animals that are excreted in urine[3]. Following period of leptospiremia 7-10 days it localizes and persists in renal tubules[43]. Transmission of leptospirosis occurred by exposure to water or soil contaminated by the urine of infected animals or by direct contact with infected animals[44], i.e., rodents, ruminants, swine and canines. The environment also considered being a source of maintenance for leptospirosis in tropical

conditions[3]. Transmission also occurs when the animal is contacted with standing water like a lake or pond. Leptospirosis in small ruminants may present in acute form with increased body temperature, anorexia depression, jaundice and anemic or hemorrhagic syndrome[44] and chronic form with impaired fertility neonatal death abortions and decreased milk outputs occurred more frequently a major economic loss[45].

A subclinical infection characterized by infertility, repeat breeding, abortion, weak lambs and stillbirths. Leptospirosis is a neglected disease that's why, its effects on animals are undetermined. The lack of study on leptospirosis in small ruminants and poor study on outbreaks and surveys contributed to limited contribution for leptospirosis in animals[3]. It determined that leptospirosis in goats a main cause of abortion showing strong symptom of the syndrome[45]. It is cared and spread in the urine of infected animals. Avoid using contaminated water isolation of aborted animals and vaccination of the animals. Serological studies elaborated that Leptospira infection in goats and sheep is common worldwide, for many years small ruminants had been considered as accidental host of leptospirosis being affected only for incidental serovars, carried by other domestic and wild species. Leptospirosis in small ruminants commonly associated with strains belonging to serogroup serovars hardjo[46]. Leptospirosis shows an important infectious disease that affects the reproduction in small ruminants[2]. Many risk factors may influence the occurrence of Leptospira infection in animals. Leptospirosis is most common in cattle, an elaborative study with sufficient analysis of those factors regarding infection in the sheep has never conducted[47]. In several countries Leptospira infection in sheep and goats is determined by serological methods. Leptospirosis seroative is 25.9% in goats while 47.4% in sheep[2]. Agglutination test is the most important use for leptospirosis in the world[3]. Diagnosis can also be made by urine test of the aborted dam, aborted placenta and fetus. Vaccination play in a key role for control of leptospirosis in the herd[5].

Preventive Measures - Avoid using leptospira contaminated water as a drinking water for healthy. Isolation of animals ill or aborting from vaccinated animals. Vaccination plays an important role in the control of leptospirosis and may reduce significantly occurrence of clinical symptoms (abortions) in herd. Control of leptospirosis in small ruminants involves measures such as identification and treatment of carriers and other sources of infection. Quarantine is necessary for new herd/flock[5]. Burn or bury aborted products. Wear rubber gloves while handling tissues and fluids[3].

Q fever

Q fever is a ubiquitous zoonotic disease caused by pathogen *Coxiella burnetii* responsible for acute and chronic clinical signs[48] especially in sheep and goats causing abortion, anorexia and lesion. Cattle, sheep and goat are primary reservoirs[49]. *Coxiella burnetii* is a small obligate intracellular gram-negative that is prevalent throughout the world. Genus Coxiella a classified based on the gene sequence analysis in order of Legionellales family Coxiellaeceae with Rickettsia and Aquicella. This agent has highly osmotic resistant[50]. Ranch animals and pets are the key reservoirs of infection and transmission to human beings is mainly able through inhalation of contaminated aerosols, this bacteria also shed in milk, urine, feces, placental debris and amniotic fluid and causing illness associated with a wide clinical spectrum from asymptomatic to fatal disease[51]. Mostly introduction of bacteria is through aerosol route in farm animals[52]. To prevent from oral infection with *C. burnetii* in human is required to pasteurize the milk before use[53]. In small ruminants mainly causing abortion and stillbirth in late pregnancy without clinical signs[49]. *Coxiella burnetii* on inoculation to pregnant goats the trophoblast cells of the allanto-chorion are primary target cells for *C. burnetii*[54]. Almost in all cases trophoblasts of inner-cotyledons allantochorion and also the base of cotyledonary villi are affected[55]. Abortion in dairy goat increased by incidence of metritis. Abortion mostly occurs with no proceeding clinical signs[53]. Many studies indicate that human Q fever risk factors are more living near to farm has a history of abortions through *C. burnetii*[56]. In small ruminants premature birth, weak offspring deliver, stillbirth and abortion are reported[53]. Chronic fatigue is infrequently also associated with *C. burnetii* infection[57]. It is yet not clear that *C. burnetii* is present other than placenta or not[54]. Induction of long-lasting immune response against many diseases is facilitated by *C. burnetii*. Immune response to *C. burnetii* infection is better studied in goats than in sheep[58] but result from work in goats could also be applicable in sheep.

After inoculation of *C. burnetii* specific antibodies both IgM, IgG can be detected after two weeks and remained for up to 13 weeks. Prevalence of *C. burnetii* in sheep or goats have been described on the basis of analysis different body fluids and tissues, seroprevalence have been described for many countries but these data are difficult to compare because of the differences of the methodology of studies[15]. Sheep, goats and cattle are common hosts but many other species may be infected. Excreted in milk, urine, feces and with especially high numbers in the birth fluids and fetal membranes. Ticks can assist as a reservoir and also spread the disease (Seshadri et al., 2003). *C. burnetii* is also transmitted between sheep, goats, cat, cattle and dogs by biting of ticks or by contact with contaminated excreta. Prevention, burn or bury the reproductive organs and fluids. Infection in closely confined animals is almost universal. The level in research flocks can be reduced by periodically testing their serum and culling all infected animals (Gikas et al., 2001). This disease is present at worldwide level affecting a wide range of domestic and wild animals[59]. The presence of *C. burnetii* is worldwide except in New Zealand[60]. In many countries Q fever is epidemic in rural outbreaks and occupationally it is endemic[61]. No ovine abortion is observed in human Q fever outbreak related to sheep[62]. Analysis of human Q fever outbreak indicates that it is related to small ruminants instead of cattle[63]. In humans *C. burnetii* infection unnoticed and with signs flu-like illness, pneumonia, or as hepatitis. In 1 to 5% cases disease proceed to chronic stage mainly to endocarditis or vascular infections. A few studies have been done on ruminants and zoo animals for clinical demonstration, despite having zoonotic importance occurrence of infection information is scarce[64].

European Commission concern about the high risk of Human Q fever associated with small ruminant herds in urban areas[65]. Q fever incidence and prevalence is still not well known and undetermined in many years till now[51]. Increased numbers of lambing in lambing seasons cause an increase introduction and transmission of the pathogen in the popula-

tion or small ruminants[60]. Another factor including visiting and working professionals and animal supply also cause an increase transmission of the pathogen on the farm[56]. *C. burnetii* DNA detection by PCR is done by milk tank from dairy goats having the reproduction problem. An association between *C. burnetii* and reproductive problems prevalence is reported in some studies[58]. *C. burnetii* is having a sensitivity to oxytetracycline in vitro and demonstrated to reduce the abortion rate. Globally prevalence of *C. burnetii* in mixed herd is 38.4%, in sheep herd is 37.5%, and in goats, the herd is 28.8%. While seroprevalence 74% in sheep herd in Spain[66] and Turkey 83%[59]. Overall mean prevalence was 15% in sheep and 27% in goats.

Preventive Measures - During an outbreak screening of animal is advisable with identified risk factor[48]. Eradication of Q fever from a herd is not currently straightforward for a range of reasons, including chronic infection in a small number of animals, presence of shedding, but test-negative animals are also potential for shedding of agent[67]. Reduction of excretion has been reported using a phase 1 *C. burnetii* vaccine for animals, however, this could be affected by herd infection status and the timing of vaccination[68]. To minimize human health risks, vaccination of animals must need to be conducted in combination with repeated testing. For this, first require training of health workers and laboratory staff to strengthening laboratory analysis[69].

Prevention of shedding and abortion can be achieved by vaccination. Some vaccines claim to prevent abortion and to contribute for reduction of shedding in vaginal charges, feces and milk. Vaccination seems to be most operative when administered in non-infected small ruminants before their first pregnancy[70,71]. Pasteurization of milk from infected farms is recommended to prevent oral infection of humans[51]. Placentas and foetuses should be collected, properly stored and destroyed. Wear protective clothing, although it has been demonstrated that this does not completely prevent infection for humans[72]. General hygiene measures can also reduce exposure to animals from infecting agent.

Campylobacteriosis

The main infectious agent that causes campylobacteriosis is vibriosis (Campylobacter). Campylobacter is not much investigated in small ruminants as in other farm animals. Campylobacter is isolated from ovine meat, liver, carcass, gut, and feces[73]. Carcass contamination rate is different according to the age of animal that was 94% lambs, 63% goats, 78% kids and 72% for sheep. On an average Campylobacter presence were 30% of intestinal contents and 70% of carcass and liver surface[74]. The primary agent for abortion is *Campylobacter fetus* subspecies fetus, abortion and stillbirth occurred in late pregnancy. Remove all the aborted fetus, placenta, to avoid contamination of feed and water of other uninfected animals. It causes abortion in sheep but occasionally affects goats; *Campylobacter fetus* is a primary agent. It causes abortions and stillbirths in late-term pregnancy. It causes inflamed placenta, necrotic cotyledons, and the leathery area between cotyledons. It is spread by the aborted fetus, tissues and all discharges. Moreover, the digestive tract is probably a long term reservoir. Campylobacter is a gastrointestinal bacterial pathogen that is commonly reported in human by European Union[51]. For human infection it is confirmed by the 72-78% of sheep liver and carcass in comprised of campylobacter[75]. Human campylobacteriosis is highly acquired by consuming undercooked contaminated foods[76]. Carcass and liver of animal become colonized by Campylobacter once exposed to a contaminated external environment but remain mostly asymptomatic intestinal carriers[77].

According to EFSA, existing data on Campylobacter in goats and sheep are primarily from clinical investigations since no surveillance so far has been carried out. Moreover, the largest goat population and the fourth largest sheep population in the EU[51]. The majority of sheep and goats at slaughter carried Campylobacter present on meat and liver. This indicates that meat and offal not only of sheep but also of goat origin are commonly contaminated with a diverse population of thermophilic campylobacters, and serve as a vehicle for human infection (Lazou et al., 2014). Revealed resistance to tetracycline (47.9%) monitored by streptomycin (22.9%) and ciprofloxacin alongside nalidixic acid (18.3%) Isolates exhibited low opposition to erythromycin (2.5%) and were liable to gentamicin[74]. Now vaccines are available to prevent Campylobacter infections.

Preventive Measures - Ovine vaccines are available but should be used prior to exposure. They may not protect for all kinds of strains. Antibiotics can be fed prophylactically during pregnancy (tetracycline at 100 mg/head/day). Feed in mangers and water in troughs to avoid contamination of feed and water by aborted material of infected animals. Remove aborting ewes, fetus, and placenta from lambing area. Parenteral injection of oxytetracycline (antibiotic) followed with repeated injections, will decrease the abortion loss.

Brucellosis

"Malta fever" now called brucellosis firstly came from British during Crimean War[6]. Brucellosis is having zoonotic importance worldwide high impact on rural livelihood and underestimated toward febrile illness[78]. The economic and public health impact by brucellosis is considered the main concern in developing countries. This disease causes a significant loss of production by abortion, low herd fertility, stillbirth and low milk[8]. Due to zoonotic impact it leads to morbidity. It is considered most common zoonotic disease is occurring globally[79]. Brucellosis is the world's most common considered bacterial disease[80]. Brucella species are intracellular gram-negative coccobacillus that can infect many animal species including human also[81]. *Brucella melitensis* infects goats and sheep common in many countries. Primary clinical effect of brucellosis is related to production problems in livestock[6]. It is a zoonotic disease.

Brucella abortus primarily infects cattle but can infect sheep and goat also. *B. ovis* cause brucellosis with no zoonotic impact with genital lesions in rams, placentitis and abortion in ewes. The agent can be secreted by vaginal discharge and milk to other related animals in a herd. In some countries, *B. abortus* is reported in cattle[82] as well as in small ruminants[83]. But mixed infection by both has also been reported[84]. *B. melitensis* (sheep, goats, biovars1-3). *B. ovis* (sheep) among these *B. melitensis* having a high risk for human infection which is followed by *B. suis* and *B. abortus* and others are virulent for human health[85]. The serological test has been done only in sheep *B. ovis* having low affinity for the host. This disease causes abortion in late gestation, retained placenta, perhaps some weak newborn animals. It can be spread by

oral ingestion of the organism from the fetus, placenta, uterine discharges or contaminated feed and water; it can also enters through the conjunctiva, mucous membranes, wound and intact skins. In dairy farms, mostly dog use contaminated milk and carcass, aborted fetus, placenta and vaginal debris then serve as a basis of infection for canine brucellosis and can also transmit to livestock[86]. It is prevented by involving testing and testing of slaughtering of animals, isolate aborted animals, clean up and burn the aborted fetus and placenta, contaminated bedding manure. Keep all aborted tissues and fluids away from dogs and birds. Clean and disinfect floors, feed bunks, building, and equipment's. The most widely used diagnostic techniques are serological tests such as complement fixation, agar gel immunodiffusion (AGID), and indirect ELISA. Although seroreactivity to an agent does not necessarily mean that the animal was clinically affected by that pathogen. Furthermore, we inferred that these pathogens contributed to the decreased productivity of these animals[2].

Quarantine the new herd until further serological testing reveals no new cases. In general, brucellosis causes huge loss of production by abortion and stillbirth and low milk. If brucellosis is highly prevalent in a country then improved diagnosis can be helpful for proper treatment[78]. By regression analysis, it is reported that association of antibody against brucellosis is having high potential risk for age, history of abortion and party number for *B. melitensis* infection in small ruminants[6]. In Nigeria, reported seroprevalence is 0-76% in small ruminants and humans; it is 0-74%[69]. Brucellosis primary affects on livestock, but it can also affect humans by ingestion of contaminated milk or meat and by close contact with infected animals[87]. Animal-to-human transmission may occur through a direct connection with the vaginal and placental fluid and material and aborted fetuses of infected animals, or via consumption of raw milk or unpasteurized dairy products from these animals[69]. Brucellosis is endemic among Mediterranean countries of Europe. Northern and eastern Africa, India, central Asia, Mexico and South America almost occurred in the whole world. Signs and symptoms of brucellosis in human are not specified and be confused with febrile illness especially malaria[88]. Poor diagnosis can result in the treatment of malaria for brucellosis and unnecessary use of antimalarial medicine in human[88]. Some studies are conducted in high-risk groups like a farmer, veterinary professionals, meat inspectors and artificial insemination technicians in Amhara Regional State[86]. The importance of brucellosis in equine, swine and wild animals has also not been addressed to date[6].

Preventive Measures - Brucellosis can transmit to human by consuming unpasteurized products or direct contact with infected animals[89]. Vaccination was applied to overcome extensive bovine abortions in government-owned farms and local production by a liquid S19 vaccine started. A test and killing policy was also implemented[69]. Many countries have eradicated brucellosis by this method. Isolate the aborted animal from normal ones. Clean up and burn the aborted foetus and placenta, contaminated bedding, manure. Keep all aborted tissues and fluids away from dogs and birds. Clean and disinfect floors, feed bunks, buildings and equipment. Use serologic tests to identify infected animals and if positive for brucellosis send to slaughter.

Quarantine the new incoming animals for almost 30 days. Buy all replacement animals from herds or flocks that have been certified free of brucellosis or animals tested as serologically negative prior to bring them into new herds or flocks which are free of brucellosis.

Listeriosis

It is triggered by *Listeria monocytogenes*, a bacterial disease. Listeria species are small gram-positive rod-shaped having 1-2 micron in length and 0.5 micron width. Optimal growth temperature for these bacteria ranges from 30-37celcius. But organism can also grow and reproduce at a temperature of -0.4 and 45 celciuse with a pH of 4.5-9.6 in aerobic or microaerophilic conditions. Common in goats but sheep affected occasionally. *L. monocytogenes* is a universal organism for which soil is the most important cave for its transmission and persistence to animals[90]. The risk factor for listeriosis is associated with winter season by using silage listeria can grow at this low temperature while another pathogen cannot grow, and their growth is inhibited at that temperature. The incidence rate for this may reach 9%, but rarely it is up to 2%. It is isolated from livestock[91]. *Listeria monocytogenes* mostly distributed in soil, feces and environment of animals. Upon certain conditions, it becomes highly pathogenic and causes serious disease. It is clinically characterized by abortion, decomposed fetus, necrosis of cotyledons and necrotic foci in the lungs and liver. May have a severe uterine infection after an abortion; abortion commonly occurs during late pregnancy spread of agent by spoil silages with soil and rodent contamination. Other clinical signs for listeriosis are septicemia, abortion, mastitis and gastroenteritis. The diseased animal can shed the organism in milk and feces. It is also zoonotic one that's why infection from milk and meat is of real concern[92]. Abortions usually occurred in the last of gestation. Fever, depression, metritis may also occur in it. The main clinical sign is of nervous system unilateral or bilateral. The outbreak of listeriosis can also occur by without any silage feeding but can occur by feeding low-quality pasture or vegetation to animals. In ruminants, sheep are one of the most commonly affected one clinical characterized by encephalitis, septicemia, abortion, mastitis and gastroenteritis[92]. It can be prevented by improving the storage and management of the silage or other forages. Antibiotic can be administered for a long period be a cause of recovery period for almost one month. Prevalence of organism is higher in cattle than sheep[93]. Removal of *L. monocytogenes* is an unrealistic challenge because it can survive in very stressful conditions of the environment. But efficient management and control measure can help to reduce food contamination[94].

Preventive Measures - Make improvement in storage and handling of silages as well as forages because these are sources of infecting agent.

Trypanosoma (Dutton Ella) vivax

Trypanosoma vivax is a blood parasite that is normally associated with anemia and permanent febrile status causing a loss in production, weakness of related animals and sometime may causing the death of the infected animal[95]. Trypanosomosis is a disease of economic importance caused by blood protozoan *Trypanosoma* spp. That affects most of the areas of South America, Africa, and Central America causing a huge loss in the cattle industry. The Trypanosoma

species members are parasites having two hosts involved in their life cycle. Bloodsucking insects are the main vectors for transmission of trypanosome[96]. This parasite initially named by *T. guyanense* later on according to genetic similarity with *T. vivax* was high so considered it as a separate group of the parasite[95]. For transmission, by the natural way the vector is tsetse fly and by mechanical it is directly transmitted from one animal to other by blood-sucking parasites, i.e. Tabanidae and Stomoxydae[97]. It can also be transmitted by invertebrates which sucks blood, i.e., Vampire bats and by the mechanical way by contaminated needles by infected blood[98]. Trypanosoma caused by *T. vivax* may spread in a new herd that is never before exposed to blood-sucking parasite can also be infected within 6months[99]. *T. vivax* infection triggered by high temperature, anorexia, anemia and also degenerative changes at testicular and epididymis level[100]. It can also affect semen quality and may cause infertility or sterility (Bittar et al., 2015). It may result in multi-focal epididymitis and hyperplasia of epididymis tissue. Beside this in female sheep, *T. Vivax* also results into the degeneration of hypothalamus, hypophysis and gonads that results into hormonal disturbance and lower its concentration in blood plasma which is necessary the basic fundamental reproductive processes like gestation. These conditions might cause an increase in corticosteroid, estrogen; prostaglandins results in abortion and luteolysis[35].

Reproductive failure includes irregular oestrous, infertility, abortion, neonatal death, intrauterine infection, and also abortion in goats. If it is occurred in the last third of the gestation period may give rise to placental retention, perinatal mortality, and next to that disruption of the estrous cycle[95]. Damage by protozoa to placenta may cause a disturbance in placental progesterone secretion[35]. Diagnostic tools are important for the detection of the parasite to increase sensibility and specificity. It is of paramount status to prepare field professionally for differential diagnosis in reproductive failures[95]. Different parasitological, immunological and molecular techniques for diagnosis of Trypanosomosis. The simplest method for Trypanosomosis is by blood examination under a light microscope. Most important techniques for detection of trypanosome are ELISA, immunofluorescence PCR, and restriction fragments length polymorphic[96]. Trypanosoma gets different genetic variability during the stages of infection making it difficult for vaccination development[39].

Preventive Measures - Trypanosomosis is mostly confused with babesiosis, anaplasmosis, theileriosis, and even with erlichiosis (OIE, 2013). Diagnosis must consider the herd's history, the region's epidemiology and an adequate coordination between the veterinarian in charge and the diagnostic laboratory so this can allow to define the best sample and test available which can help identifying causative agent[102]. It is very important to eliminate possibility of iatrogenic transmission, using specific needles for each animal; plus, attention must be paid to fly control, especially in times of year when their population increase[95].

The Economic losses in small ruminants are mainly because of infectious causes are in the form of production loss, animal loss and production quality and quantity loss. Here we have given different reports of these losses for each infectious disease.

Disease	Losses	References
Brucellosis	Infertility, abortion, milk loss, zoonotic, 20% financial loss of total production system, weak new-borns	(89)(69) (79)(95) (103)
Q fever	In chronic high death rate, productivity loss, costly vaccination, abortion, stillbirth, public health issue	(104)(59) (63)
Trypanosomiosis	Abortion, repeat estrous, repeat breeding, retained placenta, delay uterine involution, infertility, mortality, sterility	(100)(95) (101)
Compylobacteriosis	Abortion, infertility, late pregnancy, stillbirth	(73)(95)
Listeriosis	Abortion, septicemia	(95)
Leptospirosis	Infertility, stillbirth, abortion	(105)
Toxoplasmosis	Meat loss due to infection, infertility, abortion	(95)(106)

CONCLUSION

These reproductive problems cause an economic loss in the world. Inadequate management and nutritional deficiencies cause poor production. All these reproductive problems should be resolved by positive improvements in nutritional, photoperiod & infectious causes to compensate these losses. These losses can be nullified by improvement in management and vaccination should be done to avoid zoonosis of some these reproductive diseases. The efficiency of small ruminants can be increased by the identification of the cause of disease, quarantine and active immunization by the commercially available vaccine. The more research is to be done in diagnosis and molecular basis of these reproductive diseases that were neglected in past. Which have made high impact on countries economy.

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References

1. Kosgey IS, Okeyo AM. Genetic improvement of small ruminants in low-input, smallholder production systems: Technical and infrastructural issues. Small Rumin Res. 2007; 70:76-88.
2. Martins G, Penna B, Hamond C, Leite RCK, Silva A, Ferreira A, et al. Leptospirosis as the most frequent infectious disease impairing productivity in small ruminants in Rio de Janeiro, Brazil. Trop Anim Health Prod. 2012; 44:773-7.
3. Martins G, Lilenbaum W. Leptospirosis in sheep and goats under tropical conditions. Trop Anim Health Prod. 2014; 46:11-7.
4. Ramzan M, Akhtar M, Muhammad F, Hussain I, Hiszczy ska-Sawicka E, Haq AU, et al. Seroprevalence of Toxoplasma gondii in sheep and

goats in Rahim Yar Khan (Punjab), Pakistan. Trop Anim Health Prod. 2009; 41(7):1225-9.
5. S Subharat, Wilson PR, Heuer C, Collins-emerson JM, Subharat S, Wilson PR, et al. Vaccination for leptospirosis improved the weaning percentage of 2-year-old farmed red deer hinds in New Zealand Vaccination for leptospirosis improved the weaning percentage of 2-year-old farmed red deer hinds in New Zealand. New Zeal vterinary J. 2011; 59(4):191-6.
6. Yilma M, Mamo G, Mammo B. Achievements in the Life Sciences Review on Brucellosis Sero-prevalence and Ecology in Livestock and Human Population of Ethiopia. Achiev life Sci. 2016; 10:80-6.
7. Dabbasa G et al. Debassa 2013.pdf. 2013. p. 14-21.
8. Roth F, Zinsstag J, Orkhon D, Hutton G, Cosivi O, Carrin G, et al. Human health benefits from livestock vaccination for brucellosis: case study. Bull world Heal Organ. 2003; 81(12).
9. Martin GB, Rodger J, Blache D. Nutritional and environmental effects on reproduction in small ruminants. Reprod Fertil Dev. 2004; 16(4):491-501.
10. Dobson H, Fergani C, Routly JE, Smith RF. Effects of stress on reproduction in ewes. Anim Reprod Sci. 2012; 130:135-40.
11. Naqvi SMK, Maurya VP, Gulyani R, Joshi A, Mittal JP. The effect of thermal stress on superovulatory response and embryo production in Bharat Merino ewes. Small Rumin Res. 2004; 55:57-63.
12. Ali A, Hayder M. Seasonal Variation of Reproductive Performance, Foetal Development and Progesterone Concentrations of Sheep in the Subtropics. Reprod Dom Anim. 2008; 43:730-4.
13. Saifullizam AK, Routly JE, Smith RF, Dobson H. Physiology & Behavior Effect of insulin on the relationship of estrous behaviors to estradiol and LH surges in intact ewes. Physiol Behav. 2010; 99:555-61.
14. Maurya VP, Naqvi SMK, Gulyani R, Joshi A, Mittal JP. Effect of Thermal Stress on Sexual Behaviour of Superovulated Bharat Merino Ewes. asian-aust.j Anim Sci. 2005; 18(10):1403-6.
15. Seegers H, Taurel A, Joly A. Prevalence of Coxiella burnetii infection in domestic ruminants: A critical review. 2011; 149:1-16.
16. Alvarez L, Martin GB, Galindo F, Zarco LA. Social dominance of female goats affects their response to the male effect. Appl Anim Behav Sci. 2003; 84:119-26.
17. Somchit A, Campbell BK, Khalid M, Kendall NR, Scaramuzzi RJ. The effect of short-term nutritional supplementation of ewes with lupin grain (Lupinus luteus), during the luteal phase of the estrous cycle on the number of ovarian follicles and the concentrations of hormones and glucose in plasma and follicular fluid. 2007; 68:1037-46.
18. Kiyma Z, Alexander BM, Kirk EA Van, Murdoch WJ, Hallford DM, Moss GE. Effects of feed restriction on reproductive and metabolic hormones in ewes. J Anim Sci. 2004; 82(February):2548-57.
19. Tanaka T, Fujiwara K, Kim S, Kamomae H, Kaneda Y. Ovarian and hormonal responses to a progesterone-releasing controlled internal drug releasing treatment in dietary-restricted goats. Anim Reprod Sci. 2004; 84:135-46.
20. Rondina D, Freitas VJF, Spinaci M, Galeati G. Effect of Nutrition on Plasma Progesterone Levels, Metabolic Parameters and Small Follicles Development in Unstimulated Goats Reared Under Constant Photoperiod Regimen. 2005; 552:548-52.
21. Long NM, Nijland MJ, Nathanielsz PW, Ford SP. The effect of early to mid-gestational nutrient restriction on female offspring fertility and hypothalamic-pituitary-adrenal axis response to stress 1. J Anim Sci. 2010; 88:2029-37.
22. Alexander BM, Kiyma Z, Mcfarland M, Kirk EA Van, Hallford DM, Hawkins DE, et al. Influence of short-term fasting during the luteal phase of the estrous cycle on ovarian follicular development during the ensuing proestrus of ewes. Anim Reprod Sci. 2007; 97:356-63.
23. Bobowiec R, Lipecka C. Fasting-induced Changes in Ovulation Rate, Plasma Leptin, Gonadotropins, GH, IGF-I and Insulin Concentrations During Oestrus in Ewes. J. vet Med A. 2006; 53:5-11.
24. Roberts AJ, Funston RN, Moss GE, Roberts AJ, Funston RN, Moss GE. DigitalCommons@University of Nebraska - Lincoln Insulin-Like Growth Factor Binding Proteins in the Bovine Anterior Pituitary Insulin-Like Growth Factor Binding Proteins in the Bovine Anterior Pituitary. 2001.
25. Selvaraju S, Agarwal SK, Karche SD, Majumdar AC. Ovarian response, embryo production and hormonal profile in superovulated goats treated with insulin. 2003; 59:1459-68.
26. C.Vinole BP, Glover KMM. The use of a 'first-wave' model to study the effect of nutrition on ovarian follicular dynamics and ovulation rate in the sheep. Reproduction. 2010; 140:865-74.
27. Leroy JLMR, Vanholder T, Delanghe JR, Opsomer G. Metabolic changes in follicular fluid of the dominant follicle in high-yielding dairy cows early post partum. Theriogenology. 2004; 62:1131-43.
28. Farman M, Nandi S, Kumar VG, Tripathi SK. Effect of Metabolic Stress on Ovarian Activity and Reproductive Performance of Dairy Cattle : A Review. 2016; 6:1-7.
29. Argov N, Sklan D. Expression of mRNA of Lipoprotein Receptor Related Protein 8, Low Density Lipoprotein Receptor, and Very Low Density Lipoprotein Receptor in Bovine Ovarian Cells During Follicular Development and Corpus Luteum Formation and Regression. 2004; 175(August 2003):169-75.
30. Miller WL, Auchus RJ. The Molecular Biology, Biochemistry, and Physiology of Human Steroidogenesis and Its Disorders. 2011; 32(February):81-151.
31. Ferreira FA, Gomez RGG, Joaquim DC, Watanabe YF. Short-term urea feeding decreases in vitro hatching of bovine blastocysts. THE. 2011; 76(2):312-319.e1.
32. Santos P, Marques A, Antunes G, Chaveiro A, Andrade M, Borba A, et al. Effects of Plasma Urea Nitrogen Levels on the Bovine Oocyte Ability to Develop After In vitro Fertilization. Reprod Dom Anim. 2009; 44:783-7.
33. Buxton D, Maley SW, Wright SE, Rodger S, Bartley P, Innes EA. Toxoplasma gondii and ovine toxoplasmosis: New aspects of an old story. Vet Parasitol. 2007; 149:25-8.
34. Puije WNA Van Der, Bosompem KM, Canacoo EA, Wastling JM. The prevalence of anti- Toxoplasma gondii antibodies in Ghanaian sheep and goats. ACTA Trop. 2000; 76:21-6.
35. Silva TMF, Olinda RG, Rodrigues CMF, Câmara ACL, Lopes FC, Coelho WAC, et al. Pathogenesis of reproductive failure induced by Trypanosoma vivax in experimentally infected pregnant ewes. Vet Res. 2013; 44(1):1-9.
36. Innes EA, Bartley PM, Buxton D, Katzer F. Ovine toxoplasmosis. 2010; (October 2009):1887-94.
37. Olivier A, Budka H, Buncic S, Colin P, Collins JD, De A, et al. Scientific Opinion of the Panel on Biological Hazards Adopted on 17 October 2007. EFSA J. 2007; 583:1-64.
38. Lashari M.H and Z Tasawar. Pakistan Veterinary Journal. Pak Vet J. 2010; 30(2):91-4.
39. Zambrano-villa S, Rosales-borjas D, Julio C, Ortiz-ortiz L, Zambrano-villa S, Ortiz-ortiz L. How protozoan parasites evade the immune response. Trends Parasitol. 2002; 18(6):272-8.
40. Oncel T, Vural G. Occurrence of Toxoplasma gondii antibodies in sheep in Istanbul, Turkey. Vet Arh. 2006; 76(6):547-53.
41. Dubey JP. Toxoplasmosis - a waterborne zoonosis. 2004; 126:57-72.
42. Adler B, Lo M, Seemann T, Murray GL. Pathogenesis of leptospirosis : The influence of genomics. Vet Microbiol. 2011; 153:73-81.
43. Grooms DL, Bolin CA. Diagnosis of Fetal Loss Caused by Bovine Viral Diarrhea Virus and Leptospira spp. Veterinay Clin. 2005; 21:463-72.
44. Adler B, Pen A De. Leptospira and leptospirosis. Vet Microbiol. 2010; 140:287-96.
45. Lilenbaum W, Varges R, Ristow P, Cortez A, Souza SO, Richtzenhain LJ, et al. Research in Veterinary Science Identification of Leptospira spp. carriers among seroreactive goats and sheep by polymerase chain reaction. Res Vet Sci. 2009; 87(1):16-9.
46. Endemicity of leptospirosis in domestic and wild animal species from Reunion Island (Indian Ocean). 2012.
47. Pacheco J, Lima-ribeiro AMC, Oliveira PR, Pacheco M, Júnior ÁF. Seroprevalence and risk factors for Leptospirosis in goats in Uberlândia, Minas Gerais, Brazil. 2012; 101-6.
48. Klaasen M, Roest H-J, van der Hoek W, Goossens B, Secka A, Stegeman A. Coxiella burnetii Seroprevalence in Small Ruminants in The Gambia. PLoS One. 2014; 9(1):e85424.
49. Brom R Van Den, Engelen E Van, Roest HIJ, Hoek W Van Der, Vellema P. Coxiella burnetii infections in sheep or goats: an opinionated review. Vet Microbiol. 2015; 181:119-29.
50. Seshadri R, Paulsen IT, Eisen JA, Read TD, Nelson KE, Nelson WC, et al. Complete genome sequence of the Q-fever pathogen Coxiella burnetii. PNAS. 2003; 100(9):5455-60.
51. Panel E, Ahaw W. Scientific Opinion on Q fever 1. EFSA J. 2010; 8(5).
52. Roest HIJ, Post J, Gelderen B Van, Zijderveld FG Van, Rebel JMJ. Q fever in pregnant goats: humoral and cellular immune responses. Vet Res. 2013; 44(67):1-9.
53. Rodolakis A. Q fever, state of art: Epidemiology, diagnosis and prophylaxis. Small Rumin Res. 2006; 62:121-4.
54. Roest H, Gelderen B Van, Dinkla A, Frangoulidis D, Van F, Rebel J, et al. Q Fever in Pregnant Goats: Pathogenesis and Excretion of Coxiella burnetii. PLoS One. 2012; 7(11):e48949.
55. Brom R Van Den, Engelen E Van, Luttikholt S, Moll L, Maanen K Van, Vellema P. Papers Coxiella burnetii in bulk tank milk samples from dairy goat and dairy sheep farms in The Netherlands in 2008. Vet recoed. 2012; 170(310).
56. Schimmer B, Schegget R, Wegdam M, Züchner L, Bruin A De, Schneeberger PM, et al. The use of a geographic information system to

identify a dairy goat farm as the most likely source of an urban Q-fever outbreak. BMC Infect Dis. 2010; 10(69):2-7.
57. Asseldonk MAPM Van, Prins J, Bergevoet RHM. Economic assessment of Q fever in the Netherlands. Prev Vet Med. 2013; 112:27-34.
58. Tavares N, Carolino N, Sidi-boumedine K, Silva GJ. Serological evidence of exposure to Coxiella burnetii in sheep and goats in central Portugal. Vet Microbiol. 2013; 167:500-5.
59. Dufour P, Kennerman E, Rousset E, Go E. Seroprevalence of Q fever (coxiellosis) in sheep from the Southern Marmara Region, Turkey Séroprévalence de la fièvre Q (coxiellose) chez les ovins de la région Marmara-Sud, Turquie. Comp Immunol Microbiol Infect Dis. 2010; 33:37-45.
60. Woldehiwet Z. Q fever (coxiellosis): epidemiology and pathogenesis. Res Vet Sci. 2004; 77:93-100.
61. Vellema P, Brom R Van Den. The rise and control of the 2007 - 2012 human Q fever outbreaks in the Netherlands. Small Rumin Res. 2014; 118:69-78.
62. Epidemiology F, Program T, Office PH, Protection C, Baden-wurttemberg SHO. Short Report Large Q fever outbreak due to sheep farming near residential areas, Germany, 2005. Epidemiology.infect. 2008; 136:1084-7.
63. Georgiev M, Afonso A, Neubauer H, Needham H, Thiéry R, Rodolakis A, et al. Q fever in humans and farm animals in four European countries, 1982 to 2010.
64. Clemente L, Barahona MJ, Andrade MF, Botelho A. Short Communications Diagnosis by PCR of Coxiella burnetii in aborted. Vet Rec. 2009; 164:373-4.
65. Panaiotov S. An outbreak of Q fever in Bulgaria. Ann Ist Super Santia. 2009; 45(1):83-6.
66. Ruiz-fons F, Astobiza I, Barandika JF, Hurtado A, Atxaerandio R, Juste RA, et al. Seroepidemiological study of Q fever in domestic ruminants in semi-extensive grazing systems. BMC Vet Res. 2010; 6(3):1-6.
67. Rousset E, Berri M, Durand B, Dufour P, Prigent M, Delcroix T, et al. Coxiella burnetii Shedding Routes and Antibody Response after Outbreaks of Q Fever-Induced Abortion in Dairy Goat Herds. 2009; 75(2):428-33.
68. Cremoux D, Rousset E, Touratier A, Audusseau G, Nicollet P, Pape M Le. Immunology & Medical Microbiology. 2012; 64:104-6.
69. Ducrotoy MJ, Bertu WJ, Ocholi RA, Gusi AM, Bryssinckx W, Welburn S, et al. Brucellosis as an Emerging Threat in Developing Economies: Lessons from Nigeria. PLoS One. 2014; 8(7):e3008.
70. Brom V Den, Schimmer B, Schneeberger PM, Swart WA, Hoek W Van Der. Seroepidemiological Survey for Coxiella burnetii Antibodies and Associated Risk Factors in Dutch Livestock Veterinarians. 2013; 8(1):1-5.
71. Astobiza I, Barandika F, Ruiz-fons F, Hurtado A. Four-Year Evaluation of the Effect of Vaccination against Coxiella burnetii on Reduction of Animal Infection and Environmental Contamination in a Naturally Infected Dairy Sheep Flock. 2011; 77(20):7405-7.
72. Workers C, Whelan J, Schimmer B, Schneeberger P, Meekelenkamp J, Ijff A, et al. Q Fever among. 2011; 17(9):2009-10.
73. Horrocks SM, Anderson RC, Nisbet DJ, Ricke SC. Anaerobe Incidence and ecology of Campylobacter jejuni and coli in animals. Anaerobe. 2009; 15:18-25.
74. Lazou T, Houf K, Soultos N, Dovas C, Iossi E. International Journal of Food Microbiology - Campylobacter in small ruminants at slaughter: Prevalence, pulsotypes and antibiotic resistance. Int J Food Microbiol. 2014; 173:54-61.
75. Strachan NJC, Macrae M, Thomson A, Rotariu O, Ogden ID, Forbes KJ. International Journal of Food Microbiology Source attribution, prevalence and enumeration of Campylobacter spp. from retail liver. Int J Food Microbiol. 2012; 153:234-6.
76. Jacobson C, Bell K, Forshaw D, Besier B. Veterinary Parasitology Association between nematode larvae and "low worm egg count diarrhoea" in sheep in Western Australia. Vet Parasitol. 2009; 165:66-73.
77. Humphrey T, Brien SO, Madsen M. Campylobacters as zoonotic pathogens : A food production perspective. food Microbiol. 2007; 117:237-57.
78. Germeraad EA, Hogerwerf L, Faye-Joof T, Goossens B, Van Hoek W Der, Jeng M, et al. Low seroprevalence of brucellosis in humans and small ruminants in the Gambia. PLoS One. 2016; 11(11):e0166035.
79. Dean AS, Bonfoh B, Kulo AE, Boukaya GA, Amidou M, Hattendorf J, et al. Epidemiology of Brucellosis and Q Fever in Linked Human and Animal Populations in Northern Togo. PLoS One. 2013; 8(8):e71501.
80. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos E V. The new global map of human brucellosis. http://infection.thelancet.com. 2006; 6(February):91-9.
81. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. review article. N Engl J Med. 2005; 352:2325-36.
82. Rahman MS, Han J, Park J, Lee J, Eo S, Chae J. Short Communications Prevalence of brucellosis and its association with reproductive problems in cows in Bangladesh. Vet Rec. 2006; 159:180-2.
83. Bekele M, Mohammed H. Small ruminant brucellosis and community perception in Jijiga District, Somali Regional State, Eastern Ethiopia. Trop Anim Health Prod. 2011; 43:893-8.
84. Mcdermott JJ, Arimi SM. Brucellosis in sub-Saharan Africa: epidemiology, control and impact. Vet Microbiol. 2002; 90:111-34.
85. Godfroid J, Scholz HC, Barbier T, Nicolas C, Wattiau P, Fretin D, et al. Brucellosis at the animal / ecosystem / human interface at the beginning of the 21st century. Prev Vet Med. 2011; 102:118-31.
86. M.Yohannes et.al 2012. Bovine Brucellosis: Serological Survey in. Glob Vet. 2012; 8(2):139-43.
87. Musa MT, Eisa MZM, Sanousi EM El. Brucellosis in Camels (Camelus dromedarius) in Darfur, Western Sudan. 2008; 138.
88. Vialle-valentin CE, Lecates RF, Zhang F, Ross-degnan D. Treatment of Febrile illness with artemisinin combination therapy: prevalence and predictors in five African household surveys. J of Pharmaceutical Policy Pract. 2015; 8(1):1-9.
89. Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. 2007.
90. Vivant A, Garmyn D, Piveteau P. Listeria monocytogenes, a down-to-earth pathogen. 2013; 3(November):1-10.
91. kuldeep Dhama KK, R.Tiwari, et al. 2015. Listeriosis in animals, its public health significance (food-borne zoonosis) and advances in diagnosis and control: a comprehensive review. Vet Q. 2015 (July).
92. Abdlla OA, Elboshy ME, Reisha EF, Gadlla HA, El-khodery SA. Cytokine in cerebrospinal fluid and outcome prediction in Ossimi sheep with encephalitic listeriosis. Cytokine. 2015; 73:283-7.
93. Esteban JI, Oporto B, Aduriz G, Juste RA, Hurtado A. Faecal shedding and strain diversity of Listeria monocytogenes in healthy ruminants and swine in Northern Spain. BMC Vet Res. 2009; 5(2):1-10.
94. Hurtado A, Ocejo M, Oporto B. Salmonella spp. and Listeria monocytogenes shedding in domestic ruminants and characterization of potentially pathogenic strains. Vet Microbiol. 2017; 210:71-6.
95. Betancur Hurtado OJ, Jimenez Castro PD, Giraldo-Ríos C. Reproductive failures associated with Trypanosoma (Duttonella) vivax. Vet Parasitol. 2016; 229:54-9.
96. Dagnachew S, Bezie M, Terefe G, Abebe G, Barry JD, Goddeeris BM. Comparative clinico-haematological analysis in young Zebu cattle experimentally infected with Trypanosoma vivax isolates from tsetse infested and non-tsetse infested areas of Northwest Ethiopia. ACTA Vet Scandinavca. 2015; 57(24):1-9.
97. Birhanu H, Fikru R, Said M, Kidane W, Gebrehiwot T, Hagos A, et al. Epidemiology of Trypanosoma evansi and Trypanosoma vivax in domestic animals from selected districts of Tigray and Afar regions, Northern Ethiopia. 2015; 1-11.
98. Pecuarias C. Revista Colombiana de Ciencias Pecuarias. 2009; 25-32.
99. Paulo S, São D. First report of Trypanosoma vivax outbreak in dairy cattle in. 2012; 2961:118-24.
100. Batista JS, Rodrigues CMF, Olinda RG, Silva TMF. Highly debilitating natural Trypanosoma vivax infections in Brazilian calves: epidemiology, pathology, and probable transplacental transmission. 2012; 73-80.
101. Bittar JFF, Bassi PB, Moura DM, Garcia GC, Martins-filho OA, Vasconcelos AB, et al. Evaluation of parameters related to libido and semen quality in Zebu bulls naturally infected with Trypanosoma vivax. BMC Vet Res. 2015; 1-7.
102. Anderson ML. Infectious causes of bovine abortion during mid- to late-gestation. 2007; 68:474-86.
103. Carvalho A V, Mol JPS, Xavier MN, Paixão TA, Lage AP, Santos RL. Pathogenesis of bovine brucellosis. Vet J. 2010; 184(2):146-55.
104. Roth F, Zinsstag J, Orkhon D, Hutton G, Cosivi O, Carrin G, et al. Human health benefits from livestock vaccination for brucellosis: case study. 2003; 81(02).
105. Grooms DL. Reproductive losses caused by bovine viral diarrhea virus and leptospirosis. 2006; 66:624-8.
106. Scallan E, Hoekstra RM, Angulo FJ, Tauxe R V, Widdowson M, Roy SL, et al. Foodborne Illness Acquired in the United States - Major Pathogens. 2011; 17(1):7-15.