

MATERNAL IMMUNOGLOBULINS TRANSFER AND NEONATAL LAMB MORTALITY - A REVIEW

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ABSTRACT

The maternal immunoglobulins acquired through the colostrum play a significant role in the defense mechanism of lamb against neonatal diseases until its own immune system is primed and produces significant amount of antibodies. The absorption of these immunoglobulins from the intestine is maximum during first six hours of life and no absorption occurs 24-36 hours postpartum. Neonatal lambs with failure or partial failure of passive transfer of immunoglobulins have higher rate of morbidity and mortality. Litter size and birth weight has significant effect on the absorption of immunoglobulins and mortality rate. The concentration of these maternal immunoglobulins in circulation at 24 hours after birth can be used as an indication of immunity or susceptibility of lambs to neonatal diseases. Several tests like zinc sulphate turbidity test, sodium sulphate turbidity test, refractometry, glutaraldehyde coagulation test, latex agglutination test, radioimmuno diffusion, radioimmunoassay, electrophoresis and ELISA have been developed for determination of immunoglobulin status. Among these, zinc sulphate turbidity test is simple to perform in laboratory and refractometry under field conditions.

INTRODUCTION

The immune system of the lamb is fully developed well before birth but is in unprimed state (Tizard, 1992). The maternal immunoglobulins acquired through the colostrum play a significant role in the defence mechanism of new born lamb until its own immune system is primed and produces significant amount of antibodies. With the onset of immunoglobulins synthesis, IgG₁ is detected in the serum of colostrum-deprived neonatal lambs within a week of birth whereas appearance of IgG₂ is delayed until three to four weeks postpartum (Varela-Diaz and Soulsby, 1972). However, significant concentration of antibodies to protect against infections takes longer time and losses due to acquired neonatal infections are about 8-14.5 per cent (Johnston *et al.*, 1980; Purvis *et al.*, 1985).

Colostrum is not only rich in immunoglobulins as compared to milk (Table 1) but is also an excellent source of energy, vitamin A and essential minerals (Khan and Khan, 1996).

Lamb requires between 180 and 210 ml of colostrum/Kg body weight during first 18 hours after birth in order to provide sufficient fuel for heat production (Mellor and Murray, 1986). Eales *et al.* (1980) were of the view that adequate supply of colostrum prevents hypothermia more effectively than providing shelter. Losses due to hypothermia are much higher upto 34 (Purvis *et al.*, 1985) and 43 per cent (Johnston *et al.*, 1980). Colostrum intakes of this order usually provide enough immunoglobulins for protection against field infections. The septicemic/bacteraemic deaths are related to a deficiency of IgM whereas IgG

deficiency is associated with diarrhoea and re-excretion of IgA helps in stopping the diarrheic process (Fisher, 1980). A small amount of colostrum IgG after being absorbed is secreted in the nasal and lacrimal secretions of lambs which play a valuable role in preventing respiratory infections before active local production of IgA and IgM at 2-3 weeks of age (Wells *et al.*, 1975; Smith *et al.*, 1976). Colostrum absorption also increases the number and opsonization activity of neutrophils (Bernadina *et al.*, 1991).

Absorption of immunoglobulins

Ideally the maternal immunity should be transferred *in utero* to their foetuses so that they are brought into the world protected against the microorganisms (Fisher, 1980). Placental barriers do not allow to pass immunoglobulins from dams to the neonates in ruminants (Khan and Khan, 1991b), therefore, the lamb has to depend entirely on antibodies received via colostrum (Butler, 1973). Immunoglobulins are not detected in the serum of lambs before the first intake of colostrum (Klobasa and Werhahn, 1989), however, according to Reid (1972), Sawyer *et al.* (1977), Czarnecki *et al.* (1991) and Waelchli *et al.* (1994) traces of immunoglobulins are found in lambs serum at birth probably due to *in utero* infections.

The level of proteolytic activity in the digestive tract of young animals is low and is further reduced by trypsin inhibitors present in colostrum (Tizard, 1992). Therefore, colostrum proteins without degradation reach the small intestine where they are taken up by the epithelial cells by micro-pinocytosis and passed through enterocytes into the intestinal lymphatics and capillaries

Table 1: Concentration (mg/ml) of various classes of immunoglobulins in various body fluids of dams and neonatal lambs.

	IgG	IgM	IgA	Reference
Ewe				
Blood	21.8±0.53	1.87±0.18	0.37±0.06	Fedorov (1983)
Serum	17.80	5.06	-	Sawyer <i>et al.</i> (1977)
Milk	0.6-1	0-0.07	0.05-0.12	Tizard (1992)
Colostrum				
	40-60	4-12	1-7	Tizard (1992)
	136.80	16.02	-	Sawyer <i>et al.</i> (1977)
Neonatal Lambs				
At birth serum	0.22	0.21	-	Sawyer <i>et al.</i> (1977)
24 hr post colostrum ingestion				
Blood	24.70±0.68	3.7±0.23	1.5±0.11	Fedorov (1983)
Serum	21.31	5.58	-	Sawyer <i>et al.</i> (1977)

(Khan and Khan, 1991a). The intestine is unselectively permeable, therefore, all immunoglobulins isotypes can be absorbed (Sawyer *et al.*, 1977). However, IgA is gradually re-excreted. The permeability remains highest immediately after birth to 6 hours of life. Then immature foetal type of cells capable of transfer of intact immunoglobulins are gradually replaced by a digestive type of cells (Tizard, 1992). Smeaton and Simpson-Morgan (1985) also observed that the layer of cells responsible for absorption of colostral antibodies progressively disappears from the villi, resulting in closure which usually completes 24-36 hours after birth (Khan and Khan, 1991b). So lambs absorb intact immunoglobulins from ingested colostrum only during the first day of life (Klobasa *et al.*, 1986). Trakair and Robinson (1989), however, reported that although the small intestine of sheep is relatively mature at birth, there are still vacuolated enterocytes present for at least 2 days in distal regions where these cells possess a range of vesicle morphology which might be indicative of at least two separate routes for enterocytes handling of proteins taken up from the lumen. The localisation of immunoreactive immunoglobulins within the enterocytes, presumable of colostral or milk origin, in both proximal (non-vacuolated) and distal (vacuolated) regions, does not follow patterns which suggest orderly renewal at closure. The study suggested that closure is not solely brought about by epithelial cell replacement.

Immunoglobulins reach peak level on day 1 of lamb life, then decline during the next 3 weeks (Smith *et al.*, 1976). The decline of maternal immunoglobulins in

lamb serum overlaps with the onset of lamb immunoglobulins synthesis as renewed rises are observed for IgG₂, IgM and IgG₁, after 2, 3 and 7 weeks, respectively. IgA remained at low levels characteristic of adult sheep (Klobasa and Werhahn, 1989).

Concentration of immunoglobulins in serum of lambs at various intervals was studied after one hour colostrum feeding by Halliday and Williams (1976). They observed positive effects of second feeding on the absorption of antibodies (Fig. 1). According to Klobasa *et al.* (1994), feeding at 2 hours intervals produced maximum immunoglobulin concentration at 30 hours while 6 hours feeding intervals achieved the same maximum levels at 24 hours. Concentrations of IgG and IgM in ewe serum do not correlate with those in the colostrum as the later contains abundant amounts of immunoglobulins, with IgG being selectively concentrated over IgM (Smith *et al.*, 1975; 1976; Sawyer *et al.*, 1977).

According to Varela-Diaz and Soulsby (1972) IgG₁ is transferred into colostrum of ewe, this is why among IgG₁ and IgG₂, the former is predominant in colostrum as well as in the serum of lambs after colostrum ingestion (Schmerr and Goodwin, 1991).

All the IgG, most of IgM and about half of the IgA of colostrum are derived from serum (Tizard, 1992), the rest being produced locally in the udder by plasma cells which are located in close association with glandular epithelium (Watson and Lascelles, 1973). Passive immunization of lambs is positively related to

colostral IgG contents before suckling (Esser *et al.*, 1989). Similarly, McGuire *et al.* (1983) reported that the mean serum IgG₁ concentration in lambs was significantly lower from ewes with the lowest postpartum and presuckle colostrum IgG₁ concentrations (<30 mg/ml) than mean serum IgG₁ concentration in lambs from ewes with the highest postpartum, presuckle colostrum IgG₁ concentrations (> 110 mg/ml).

Sawyer *et al.* (1977) found no relationship between immunoglobulins in the colostrum and serum of lambs at 24 hours of age, they suggested that absorption is not restricted by amount of immunoglobulins in the colostrum but by absorption factors in the gut, provided that the amount ingested is adequate. The absorption factors in the gut includes absorption time after birth, competition between *E. coli* and immunoglobulins for common intestinal receptors and physical binding of colostral immunoglobulins by intestinal microbes within the intestinal lumen which also inhibit availability of transportable immunoglobulins (Khan and Khan, 1991a).

Colostrum production ranges from 1216 to 4493 g per ewe during first 24 hours after parturition which contains 22.21 to 86.34 g of immunoglobulins. The immunoglobulin contents of colostrum fall rapidly after the first suckling and reach a low level 36 hours after the first feed and being replaced by whey contents during this period (Shubber and Doxey, 1979). Colostrum production is related to nutritional status of ewe during pregnancy. Ewes which are well fed during late pregnancy produce more colostrum than their lambs need but in most under fed ewes, the lambs requirement for colostrum exceed the ewes production (Mellor and Murray, 1986; AL-Sabbagh *et al.*, 1995).

Neonatal lamb mortality

Failure of passive transfer of immunoglobulins to neonatal lambs has significant effect on neonatal mortality and losses due to infectious causes are positively correlated with low concentrations of serum immunoglobulins. Hodgson *et al.* (1992) reported that morbidity and mortality rates were higher in colostrum-deprived lambs (80 and 67 %) than colostrum fed lambs (20 and 13 %). According to Vihan (1986), 20 per cent of colostrum-deprived lambs die within first week of life.

Colostrum consumption by individual lamb is related to litter size. The smaller the litter size, the greater is the amount ingested (Shubber *et al.*, 1979). As the serum immunoglobulin concentration is directly related to quantity of colostrum ingested by the lamb (Esser *et al.*, 1989; Otesile and Oduye, 1990), therefore, serum immunoglobulin concentration decreases as the litter size increases (Fig. 2) (Findlay, 1973; Halliday, 1976; Logan and Irwin, 1977; Gilbert *et al.*, 1988). First born lamb from twins, triplets or quadruplets has very high immunoglobulin levels than

the single born lamb (Logan and Irwin, 1977) due to the fact that amount of colostrum produced and immunoglobulin contents increase as litter size increases (Halliday, 1976). Werhahn and Klobasa (1982) reported that losses increases with number of lambs born per ewe: singles (4.7 %), twins (10.7 %), triplets (12.5%) and quadruplets (50%) (Fig.2). Similar findings had also been reported by other workers (Harker, 1973; Petersson, 1982; Hinch and Owens, 1984; Lecrivain and Janeau, 1988).

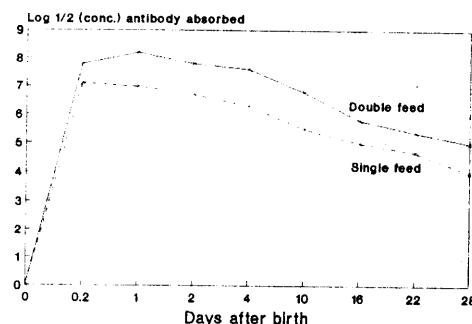


Fig. 1: Means \pm SEs of anti-egg albumin concentrations in sera from lambs given only colostrum at 1 h of age (single feed) and lambs given a second feed without added antibody at 7 h (double feed) Source: Halliday and Williams (1976).

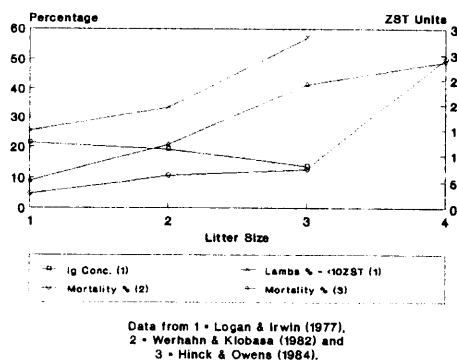


Fig. 2: Relationship of litter size with immunoglobulin concentration (ZST units), lambs (%) with less than 10 ZST units and neonatal lambs mortality.

Harker (1973) established a relationship between serum immunoglobulin concentration in lamb with that

of birth weight. The mean serum immunoglobulin concentration in lambs are 29.5 ZST units in those upto 2 Kg birth weight, 39 in 2-3 Kg, 45.6 in 3-4 Kg and 41.5 units in those over 4 Kg (Fig. 3). Highest mortality (36.8%) upto two weeks of age in lambs with low (1.5 Kg) birth weight and 10.2 % with 4 Kg birth weight was reported. Moreover, mortality rate increases (33.3%) with body weight exceeding 5.5 Kg.

According to Hinck and Owens (1984), the mortality of single, twin, triplet and quadruplet lambs were 9.0, 20.8, 41.3, and 49.1 per cent at mean birth weight of 4.6, 3.5, 2.8 and 2.4 Kg, respectively. Knight *et al.* (1988) observed that single lambs were heavier than twins, 4.98 vs 4.05 Kg and incidence of infection was higher in twins than single lambs, 4.2 vs 1.8 per cent. Similarly, Woolliams *et al.* (1983) and Purser and Young (1983) observed lamb mortality to be higher in low mean birth weights than those with higher mean birth weights. According to Ducrot *et al.* (1989) mortality was four times higher in lambs weighing < 2.5 Kg at birth than in lambs weighing over 2.5 Kg. Lambs with birth weight of 3.5 Kg and above survive best (Dalton *et al.*, 1980).

Absorption of immunoglobulins with relation to sex is controversial in literature. Sawyer *et al.* (1977) reported that immunoglobulins concentration was slightly higher in female than male lambs 24 hours after colostrum ingestion. Similarly, the mortality rate was higher in males than in females, 4.82 vs 3.92 (Khan, 1990), 59.38 vs. 46.92 per cent (Shrivastava *et al.*, 1983) and 8.83 vs. 8.69 per cent (Juma *et al.*, 1974). On the other hand, Halliday and Williams (1979) reported more efficient immunoglobulin absorption in males than females. Cinpercescu (1977), however, was unable to find any relationship between sex and immunoglobulin absorption. Similarly, Malik *et al.* (1980) and Poonia *et al.* (1983) were unable to find any significant relation between sex and survival.

There is a wide distribution in the level of circulating maternal immunoglobulins 24 hours after the ingestion of colostrum and quite a large proportion of lambs are hypogammaglobulinaemic, < 10ZST units (Reid, 1972).

According to Bekele *et al.* (1992), failure and partial failure of Ig transfer from dam to lambs are observed in 1.8 and 15.3 per cent lambs, respectively. Passive transfer failure was observed in 14 per cent apparently healthy lambs and in 46 per cent of lambs dying of natural causes between 24 hours and 5 weeks of age (Sawyer *et al.*, 1977). The results of Logan and Irwin (1977) show that 20.2 % lambs were hypogammaglobulinaemic and were more susceptible to neonatal diseases. Findlay (1973) observed that all lambs with immunoglobulins less than 20 ZST units die during first week of life. Mortality in lambs with 20-40 ZST units was very low and no mortality in lambs with 50 ZST units. According to Reid (1972), 5.5 per cent

lambs with concentration of less than 10 ZST units are likely to die during first week of life (Fig. 4). Villar and Vulich (1980) reported that 0-20 ZST units is indication of high risk of subsequent death in lambs, nearly 20 per cent of all lambs fall within this range at the age of 48 hours and 40 per cent at 7 days of age.

Study in neonatal calves also demonstrated that neonates with a serum ZST values < 20 units are very susceptible to diseases (Gay *et al.*, 1965). According to Khan (1995) mortality was three times in buffalo and cow neonates having intermediate IgG₁ concentration (0.41-1.69 g/dL) and as high as nine times in neonates with low IgG₁ concentration (< 0.4 g/dl) as compared to neonates having high IgG₁ (> 1.7 g/dl). Esser *et al.* (1989) reported that mean serum IgG contents at 24 hours after suckling in lambs those died were lower (25.3±15 mg/ml) than in those survived (33.1±15.1 mg/ml).

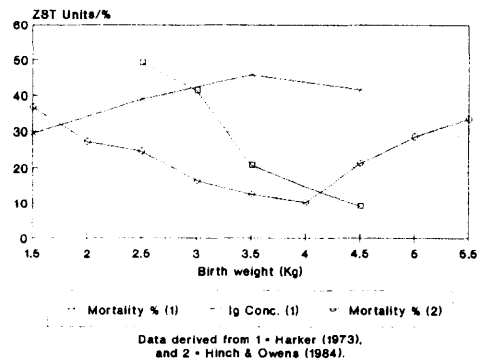


Fig. 3: Relationship of immunoglobulins concentration (ZST units) and mortality (%) with birth weight of lambs.

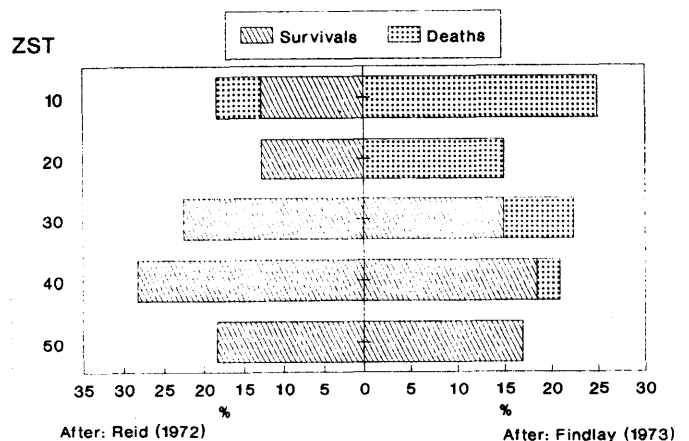


Fig. 4: Relationship of serum immunoglobulins with survival and mortality rates of neonatal lambs during first week of life.

McGuire *et al.* (1983) observed that 45 per cent lambs die before 3 weeks of age with < 6 mg/ml of immunoglobulins in their serum at 24 to 36 hours of age as compared to 5 per cent of those lambs with adequate passive transfer of immunoglobulins. Immunoglobulins concentration in serum of lambs those died was 9.2 and 1.4 mg/ml of IgG₁ and IgM compared with 36.2 and 6.1 mg/ml, respectively, in surviving lambs (Werhahn and Klobasa, 1982).

Determination of hypogammaglobulinaemia

Several tests like zinc sulphate turbidity (ZST) test, refractometry, glutaraldehyde coagulation test (GCT), latex agglutination test (LAT), radio immunodiffusion (RID), radioimmunoassay (RIA), electrophoresis and ELISA have been developed for determination of immunoglobulins status of neonates.

The ZST test is simple to perform and can be correlated with the immune status of the lamb (Reid, 1972; Logan and Irwin, 1977; Findlay, 1973; Harker, 1973). Serum hemolysis is the only serious problem encountered with ZST (Gitter and Stone, 1969).

The ZST test is simple to use in the laboratory but at the farm the refractometer can easily be used which gives the reading of total protein in the serum or plasma. As the level of albumin is fairly constant in young lambs, so the instrument indirectly gives an indication of the amount of globulin present. There is a positive correlation between values obtained by this method and those obtained by standard ZST method (Reid and Clifford, 1974; Reid and Martinez, 1975).

Pfeiffer *et al.* (1977), Naylor and Kronfeld (1977) and Rea *et al.* (1996) compared the single RID, ZST, serum electrophoresis and refractometer methods for the quantitation of calf immunoglobulins. They found that single RID proved useful for quantitation when either class or subclass information are needed. Zinc sulphate turbidity measurements gave accurate results for total immunoglobulin concentration.

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