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### Review article

## Immunoglobulin in colostrum and health of newborn Calves

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### ABSTRACT

Cow's colostrum contains the basic alimentary constituents; fat, protein, carbohydrate, minerals and vitamins, in addition to immunoglobulin, biological factors, hormones and other biological particles. These constituents play an important role in immunity and health of the newborn calves, as they are born with weak immunity and acquire their immunity after birth within three weeks continuously after being fed the colostrums. Feeding colostrums immediately after birth is found to protect the calves from the pathological factors which are around them at birth and at the beginning of breath. The synthesis of the colostrum takes place at the end of pregnancy during the dry period after increasing the hormones receptors on the epithelial cells in the udder. Colostrum production continues after birth for five days and it is the source of immunoglobulin G (IgG) and a part of IgA, IgM, in colostrums is the blood, whereas the plasma of the epithelial cells in udder synthesizes 50% of IgA and IgM. IgG forms the greatest part in colostrum approximately 85-90% and the remaining parts are IgM at rate 7% and IgA at rate 5%. Controlling udder within the dry period is basic to prevent inflammation especially subclinical mastitis, because it will lead to retard the

colostrum quantity after birth and decrease its concentration of Ig especially IgG. It is important to determine immunoglobulin level produced after birth using different methods especially the field ones, which are simple and available. These methods will help to categorize and freeze the good quality surplus colostrum to feed the newborn of low quality colostrum producing cows.

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## **1. Introduction**

The recent emphasis of immune-biochemical studies on the first weeks of calves' lives was obviously increased. Immunoglobulin plays the key role against infections occurring during early age period of calves which may lead to death. Umbilical infections and pneumonias are among the most important diseases that threaten calves. Calves mortality in dairy farms is most important irrespective of the dairy farms modernizations and reasons worldwide (Weaver et al., 2000). Of the main reasons that lead to increase mortality rates were insufficient birth cares during suckling and rearing periods (Jahnke, 2002). In Germany mortality rates increased from 5.2% in 1991 to 12.2% in 2001 (Jahnke, 2002), and it reached 20% in first lactation delivered calves. High mortality rates might lead to high economic losses due to scarcity of fattened males and females' calves, also culling of cows whose calves were dead after dystocia as they became infertile, late in pregnancy and produce less milk.

## **2. Reasons of newborn calves' mortality**

According to Kolb and Seehawer (2002) the reasons of death of newborn calves are:

- I- retardation of growth due to deficiency of ration energy, crude protein, vitamins A, E and selenium during pregnancy in addition to weakness of dams.
- II- Inability of suckling and colostrums feeding, especially after difficulty in birth which lead to insufficiency in Oxygen in the brain (Hypoxia) and the end result is deficiency in immunoglobulin.
- III- Shortage or absence of anti-bodies in colostrum, especially against pneumonias, umbilical and bowel infections.
- IV- Presence of calves in cold pens with increasing loss of body heat and consequently less colostrum feeding.
- V- Disturbance of cow metabolism (Ketosis, fatty liver syndrome) and other diseases that lead to retreat in colostrum composition and yield after birth.
- VI- Mastitis which may alternate colostrum quality and consequently its feeding.

## **3. Importance of colostrums in safety and health of newborn calves**

Calves are born virtually without Igs; therefore the colostrum Igs are essential for survival (Marnila and Korhonen, 2011). Shortage or delayed colostrum feeding play a significant role in decreasing immunoglobulin proteins in calf blood (Hypogammaglobulinemia) (Kolb, 1981; Levieux and Ollier, 1999). It has been noticed that delay in colostrum feeding will lead to shorten the period of immunoglobulin absorption in the intestine (Baumrucker and Bruckmaier, 2014). It is known that calves consumed insufficient amount of colostrums when subjected to difficulty in birth accompanied with decrease in brain oxygen (Hypoxia). It was advised in such a case to offer colostrum at a rate of 2 Liters two hours after birth, then after 12 hours using stomach tube (Kolb and Seehawer, 2002). Early feeding of colostrum is considered to be the basic source of immunoglobulin (Rajala and Castren, 1995) and in the calf, the absorption is non-selective during the first 12–36 h after the parturition (Marnila and Korhonen, 2011).

Rearing and nourishing cows during pregnancy are most important for the health and life of the new born. Shortage of energy and protein will lead to retard the growth and development of the newborn immune system (Thymus, spleen and lymph glands), which remain weak and that will lead to either early mortality of the calf or remain alive with weak performance and consume little colostrum. It was also noticed that such calves benefit a

little from Vitamins A, D3 and E in colostrum and that will lead to retard the development of the immune system (Kolb and Seehaer, 2002). Healthy pregnant cows normally produce calves with low level of immunoglobulin in blood and will acquire immunoglobulin during the first three weeks after delivery and continually through feeding colostrum. Feeding and absorption of colostrum in appreciable quantities is more important in activating the immune system and destruction of the diseases causal agents in the first weeks after birth (Baumrucker and Bruckmaier, 2014). Presenting colostrum immediately after birth will prevent the calf from diseases like *E. coli* infection and others. Besser et al. (1991) indicated that feeding colostrum in the first 24 hours after birth was not sufficient and offering colostrum in a rate of 2.84 L/animal immediately after birth using stomach tube or in a rate of 1.9 L/animal immediately after birth, 12 hours and 24 hours using bottle feeding elevated the immunoglobulin (IgG<sub>1</sub>) in blood serum to 100% compared to those suckled without assistance (Table 1).

The study indicated that colostrum should be fed immediately after birth in a rate of 2 L and 2 L after 12 hours using stomach tube (oesophageal intubation) or bottle feeding. The absorbed immunoglobulin from colostrum reaches 200 mg until 12 hours after birth and 400 mg 24 hours after birth (McGuirk, 1998). The level of IgG of 10 mg/L or more in blood plasma during the first 24 hours after birth is a good indicator of the consumed immunoglobulin (Quigley and Drewry, 1998). The study of Perino et al. (1995) showed that in standard calves rearing stations, 11 to 31% of them the level of immunoglobulin in blood plasma was low. In such calves were 9 times at risk of infections, compared to healthy ones. In addition to that mortality rate was increased 5 times. It was also noticed that immunoglobulin was low in 18.3% of calves fed colostrum with concentration of IgG less than 100 mg in the first 12 hours (Levieux and Ollier, 1999).

**Table 1**

Concentration of immunoglobulin (IgG<sub>1</sub>) in colostrum (mg/L) and in blood serum (mg/L) in calves 48 hours after birth according to methods of colostrum feeding (Besser et al., 1991).

Method of colostrum feeding	Number of calves	Level of IgG <sub>1</sub> in colostrum	Number of calves	Level of IgG <sub>1</sub> in blood serum
Natural suckling	92	21.7 ± 46.7	77	8.4 ± 10.7
Stomach tube	327	22.0 ± 25.9	334	8.7 ± 19.8
Bottle feeding	77	26.9 ± 53.1	77	10.9 ± 21.2

#### 4. Colostrum synthesis (colostrogenesis)

Colostrogenesis mostly takes place in the last day's ante-partum during the dry period (Bruckmaier, 2007), when the increase of hormonal receptors in the epithelial cells of the udder could be noticed. Prolactin and growth hormones stimulate the suitable enzymes for the formulation of triglycerides, lactose and casein. Under influence of such hormones formulation of proteins and division of epithelial cells will increase. Under optimum nutritional conditions during pregnancy, the growth and development of the udder will be stronger to the extent that synthesis of colostrum will be normal and the metabolic disorders like fatty liver syndrome and ketone bodies formation will disappear. Delouis (1978) stated that colostrum secretion takes place at the end of pregnancy and when the level of progesterone hormone was highest in blood, before it starts to decrease with the increase in estrogen level, after few hours the prolactin increased significantly with cortisol. The decrease of progesterone level and increase of prolactin is the main source of immunoglobulin proteins production. At delivery, the calf is able to consume colostrum with high nutritional and immune values necessary for its life and continues to take colostrums after birth and for five days. Mielke et al. (1994) declared that colostrum is different in composition from milk in its content of nutrients and immunoglobulin (Table 2).

The above mentioned components formed in the epithelial cells of the udder, whereas blood is the direct source of immunoglobulin IgG, part of IgA and IgM. During colostrum period the plasma of the udder epithelial cells synthesizes 50% of IgA and IgM (Kolb and Seehaer, 2002). The transfer of IgG from blood plasma to the milk follicles takes place after connection with its receptors on the epithelial cells. During the end of the dry period the numbers of the receptors are 5000 more than the natural number. The average numbers of immunoglobulin receptors are 30000 according to Sasaki et al. (1977). Since immunoglobulin is different with respect to the type of infection to which the pregnant cow is subjected, the type of antibodies could be raised according to the vaccine used against infection like *E. coli*, Clostridia, Rotavirus, Parvovirus and Rhino-tracheitis infections and that should be in the third part of the pregnancy which will lead to increase the quality of antibodies in colostrums. When

calves fed colostrum in appreciable amount they will be protected against such infections. It could be noted that in the presence of *E. coli* in small intestine before feeding colostrums, the absorption of immunoglobulin will be slow because of the denatured toxins in the intestinal epithelial cells and the effect of protease in digesting part of immunoglobulin, that confirm the importance of feeding colostrum immediately after birth (Kolb and Seehaw, 2002). A group of researchers found that colostrum yield was different with difference of cattle breed (Table 3); it was lower in first lactation compared with the latter lactations (Kruse, 1970; Levieux and Ollier, 1999). Pritchett et al. (1991) confirmed that the concentrations of immunoglobulin were generally correlated with the yield of colostrum. They also, noticed that high yielding cattle breeds produced high levels of immunoglobulin (Table 3). A number of researchers showed that season of lactation, breed and length of dry period were significantly affecting the yield of colostrum and concentration of immunoglobulin (Muller and Ellinger, 1981; Pritchett et al., 1991). Resuming milking before delivery was found to reduce the level of immunoglobulin in colostrum after delivery (Logan et al., 1981). Petrie (1984) stated that the ordinary secretion of colostrum before or during delivery was found to affect the concentration of immunoglobulin. In addition to that late secretion of colostrum or selenium deficiency and thermal stress were clearly influencing the concentration of immunoglobulin in the produced colostrum (Kruse, 1970; Sweker et al., 1995; Nardone et al., 1997). It could be noted that a positive correlation between IgG1 in the milk and lactation number, stage of lactation, daily milk production and somatic cell count and Lactation number had the highest positive direct relationship with IgG1 concentration (Liu et al., 2009). Caffin et al. (1983) showed that the immunoglobulin G<sub>1</sub> concentrations increased at the end of lactation and in samples collected from cows beyond the third lactation. There were no significant differences in immunoglobulin isotype concentrations due to genetic group (Guidry and Miller, 1986) The concentration of different Ig classes in milk and colostrum varies considerably according to species, breed, age, stage of lactation, and health status (Marnila and Korhonen, 2011). Knowledge of immunoglobulin concentration in colostrum is important in determining the amount of colostrum to be fed. As most of livestock keepers offer colostrum without knowing the concentration of immunoglobulin in it (United States Department of Agriculture, 1993).

**Table 2**

Energy and different nutrients composition of colostrum and milk during the first days of lactation (Mielke et al., 1994).

Component	Colostrum period			Milk period
	1 <sup>st</sup> day	2 <sup>nd</sup> day	3 <sup>rd</sup> day	21 <sup>st</sup> day
Energy level (MJ/kg)	5.2	4.2	3.6	2.9
DM (%)	21.6	16.9	14.2	12.3
Fat (%)	3.3	4.9	4.7	3.5
Crude protein (%)	14.2	7.4	4.3	3.3
Casein (%)	5.2	3.8	3.2	2.7
Whey protein (%)	9.0	3.6	1.1	0.6
Lactose (%)	2.9	3.7	4.4	4.8
Minerals (%)	1.2	0.9	0.8	0.7

**Table 3**

Colostrum Yield (Kg) and its content of immunoglobulin (mg/L) in Danish Friesian (Black and White) and Red Danish in relation to lactation number (Kruse, 1970).

	Lactation number		
	1 <sup>st</sup>	2 <sup>nd</sup> and 3 <sup>rd</sup>	4 <sup>th</sup> - 7 <sup>th</sup>
<b>Colostrum yield (Kg)</b>			
Danish Friesian	3.3	6.7	6.6
Red Danish	5.2	9.1	8.2
<b>Immunoglobulin Level (mg/L)</b>			
Danish Friesian	69	70	77
Red Danish	48	53	80

## 5. Importance of immunoglobulin in colostrum

Immunoglobulins as mentioned earlier are antibodies, which have the ability to conjugate with antigens and stored in phagocytes where their receptors are found. Immunoglobulins contain antigens bonds which could be 2, 4 and 10 bonds to IgG, IgA and IgM respectively. In cattle two types of IgG immunoglobulin were found, which are IgG<sub>1</sub> and IgG<sub>2</sub> depending on the properties of each. Mielke, (1994) declared that immunoglobulin in cow colostrum were different and estimated to be 85-90%, 7% and 5% of IgG, IgM and IgA respectively (Table 4).

Levieux and Ollier (1999) found no difference in average IgG concentrations of Holstein Friesian colostrum that was taken in the first milking compared to other studies; it was 59.8±28.5 mg/ml although there was a large variation in IgG concentration in colostrum which was 15.3 and 176.2 mg/ml. It was known that the highest concentration of immunoglobulin in colostrum will be immediately after delivery and decrease steadily thereafter (Stott et al., 1981). Kolb and Seehawer (2002) explained the reason to slow transfer of immunoglobulin from blood to milk follicles and its less synthesis in udder (Table 5).

Baumrucker and Bruckmaier (2014) indicated that the neonatal dairy calf's ability to absorb immunoglobulins from colostrums is assisted by a 24 h where large proteins pass the intestinal epithelial cells, but the problem many calves do not achieve the optimum because of poor quality colostrums.

**Table 4**

Average immunoglobulin concentration in Blood Plasma, Colostum and Milk (Mielke, 1994).

Fluid	Number of samples	Immunoglobulin concentration (mg/ml)			
		IgG1	IgG2	IgA	IgM
Blood Plasma	544	11.2	9.2	0.37	3.05
First Colostrum	285	46.4	2.87	5.36	6.77
Whole Milk	191	0.58	0.05	0.08	0.09

**Table 5**

Immunoglobulin concentration (mg/L) in colostrum from birth to 8 hours.

Colostrum sampling after birth(hour)	IgG <sub>1</sub>	IgG <sub>2</sub>	IgA	IgM
1	69.6	6.4	4.1	6.5
2	35.5	3.6	1.8	3.2
3	17.1	2.3	0.9	1.6
4	8.5	1.3	0.4	0.8
5	3.8	0.7	0.2	0.3
6	2.5	0.5	0.2	0.2
7	2.1	0.4	0.2	0.2
8	1.8	0.3	0.2	0.2

## 6. Mechanism of immunoglobulin proteins absorption

The epithelial cells of the intestine especially in the ileum and jejunum regions in newly born calves contain the ability to absorb the immunoglobulins molecules directly without changes. Colostrum is known to contain trypsin-inhibitor which prevents digestion of immunoglobulin proteins, in addition to the fact that at day one post-partum, abomasums produces low quantity of mineral acids which do not greatly affecting immunoglobulin proteins. It has been noticed that in 10 hours after birth the percentage of the transferred immunoglobulins from stomach epithelial cells to the blood and lymph reach about 25%. Kolb and Seehawer (2002) declared that absorption in the epithelial cells of the intestinal villi takes place in accordance with cellular absorption (Pinocytosis) and the percentage of the absorbed immunoglobulins were correlated with the time of colostrum feeding after birth. In Table (6) Kruse (1970) showed that the percentage of absorbed immunoglobulins increased with early feeding of colostrum.

**Table 6**

Percentage of immunoglobulin proteins absorption according to time of colostrum feeding after birth (Kruse, 1970).

<b>Colostrum Feeding (Hours)</b>	<b>2</b>	<b>6</b>	<b>10</b>	<b>14</b>	<b>20</b>
Quantity of Fed Colostrum L	2.2	2.7	2.6	2.9	2.9
Immunoglobulins Content of Colostrum (mg/L)	75	63	65	53	63
Percentage of Colostrum Absorption (%)	24	22	19	17	12

## 7. Mastitis and colostrum quality

Maunsell et al. (1998) clarified that dry cow mastitis clearly affected the yield of colostrum with a low level of immunoglobulin IgG<sub>1</sub>, fat and protein compared to healthy cows. Mastitis occurred during dry period was mostly sub-clinical and continued until delivery and commence of lactation (Smith *et al.*, 1985). That means sub-clinical mastitis observed in last two weeks of pregnancy occurs in the colostrogenesis period which lead to decrease in colostrum quantity and quality including concentration of immunoglobulin proteins. Immunoglobulin G in colostrums is inversely related bacterial infection at early lactation in cows (Leitner *et al.*, 2008). Some studies showed that *Staphylococcus aureus* infection occurred during colostrogenesis led to less ability of the udder epithelial cell to synthesized and secrete colostrum and with low concentration of  $\alpha$ -lacto-albumin (Sordillo et al., 1989; Larson et al., 1992). Caffin et al. (1983) showed that uninfected quarters had a mean immunoglobulin G<sub>1</sub> concentration of 46 mg/ml. This was less than means from quarters infected by minor or major pathogens. Colostrum produced by infected udder had low density. Density is considered to be a standard for immunoglobulin in colostrum (Fleenor and Stott, 1980).

## 8. Milk immunoglobulin for health promotion

The biological function of bovine colostrum immunoglobulin is to provide the newborn calf with adequate passive immune protection against microbial infections (Baumrucker and Bruckmaier, 2014). Immunoglobulin preparations designed for farm animals are commercially available, and some colostrum-based products are marketed for humans as dietary supplements. The concentration of specific antibodies against a certain pathogenic microorganism can be raised in colostrum and milk by immunizing cows with this pathogen or its antigen. Advances in bioseparation and chromatographic techniques have made it possible to fractionate and enrich these antibodies and formulate so-called hyperimmune colostrum or milk preparations. Their efficacy in prevention and treatment of various microbial infections has been evaluated in numerous studies (Mehra, et al., 2006). Immune milk preparations have proven effective in prophylaxis against infections caused by a variety of gastrointestinal pathogens. Their therapeutic efficacy, however, seems more limited. The Ig fraction of milk is utilized commercially as feed supplements and replacers of colostrums, mainly for neonatal calves in order to prevent gastrointestinal infections. Increasing interest has recently been focused on the development of colostrum-based Ig products which contain specific antibodies for the prevention or treatment of infections in humans (Marnila and Korhonen, 2011).

## 9. Methods of determining immunoglobulin level in colostrum

There are different methods used for determining immunoglobulin in colostrum, including the simple field methods and the precise laboratory methods. The former will be tacked in this review, because it is simple, cheap, fast and easy to be implemented.

### 9.1. Kruuse colostrum densimeter (Kruuse, 2002)

Used to determine colostrum density, from which the quality of colostrum can be determined. Density of colostrum is correlated with the content of immunoglobulin. Less dense colostrum contains low quantity of immunoglobulin IgG and it is of low quality. In reverse high dense colostrum contains high level of immunoglobulins, although the density can be elevated due to presence of other proteins and minerals.

## 9.2. Colostrum Bovine IgG Midland Quick Test Kit (MBC Midland Bio-Products, 2004)

Considered to be simple and fast in determining immunoglobulin (IgG) in cow colostrum.

## 10. Conclusion

According to the above mentioned the following suggestions could be explained:

- Rations rich in energy, protein, vitamins and minerals should be fed to pregnant cows, which could directly affect the growth of newborn and composition of colostrum that contains appreciable quantities of immunoglobulin.
- Colostrum should be fed immediately after birth to ensure feeding the required quantity.
- Periodical assessment of colostrum for determining the level of immunoglobulin, surplus colostrum can be frozen for nourishing calves whose mothers produce low quality colostrum.

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