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**REVIEW ARTICLE**

# ASSOCIATIONS AMONG *BETA-LACTOGLOBULIN* GENOTYPES AND SOME PRODUCTION TRAITS IN SHEEP: A SYSTEMATIC REVIEW AND META-ANALYSIS

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## ABSTRACT

Researchers have found contradictory evidence for the association between *beta-Lactoglobulin* (βlg) polymorphism and certain production traits in sheep. The aim of the study is to explore the use of meta-analysis using different genetic models in relations to βlg polymorphism in sheep for the purpose of investigating the association among βlg genes and certain production traits, such as total milk yield, fat, protein, casein and lactose content. As a result of the analysis, the association between βlg genotypes, protein and casein content was determined to be statistically significant ($p<0.05$). It was found out that the mean value was superior in favor of AA genotype for total milk yield, AB genotype for protein content and casein content especially in dairy subgroup. However, the association among βlg genotypes and other yield properties was determined to be insignificant ($p>0.05$).

**Keywords:** Sheep, Meta-analysis, βlg polymorphism, genetic model, production traits.

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## INTRODUCTION

Various studies have investigated the association between different forms of milk protein genes and economic yield traits; one of the the most important among these genotypic forms is the *beta-Lactoglobulin* (βlg). The association between βlg variants and certain production traits has been examined, and the possibility to use it as a polymorphic genetic marker has been reported in different studies (Martinez *et al*., 1993; Dario *et al*., 2008; Ramos *et al*., 2009; Yousefi *et al*., 2013; Giambra *et al*., 2014; Ozmen and Kul, 2016). Nevertheless, the differences in the association in question have been determined to be insignificant by some researchers (Esenbuga, 1995; Giaccone *et al*., 2000; Mroczkowski *et al*., 2004; Michalcova and Krupova, 2009; Giambra *et al*., 2014; Rozbicka-Wieczorek *et al*., 2015; Triantaphyllopoulos *et al*., 2017) (Supplementary file).

Although numerous studies have been published on the association between βlg gene polymorphism and some economic yield traits in sheep; the results are inconsistent due to reasons such as sample sizes used in studies, breed differences, the effect of the changing environment, the interaction between genotype and environment. Therefore, the results of such contradictory studies, which are frequently repeated, do not provide any benefit to producers.

The meta-analysis is a test method that uses the results of many different studies conducted in a specific area and provides the effect of the samples with a more powerful analysis. It may be necessary to apply the meta-analysis in a specific area, especially on a number of studies are repeated and of which sample numbers are different. By combining individual studies with this analysis, insufficiencies experienced due to the limitations of the randomized design and sufficient sample size are not observed, and it is possible to achieve stronger results (DeCoster, 2004; Borenstein *et al*., 2009).

Furthermore, the meta-analysis performed represents a good example of obtaining clearer results by the combination and analysis of the study results, which are independent of each other in a particular field, and of contributing to explaining similar or different findings in the studies.

The aim of the present study was to conduct a meta-analysis on the results of the previous studies on sheep in the literature to analyze the overall association between βlg gene and specific yield traits.

## MATERIALS AND METHODS

**Materials:** Scanning of the studies examining the association among βlg polymorphism and yield traits in databases (Web of Science, Science Direct, Google Scholar) was performed, and 22 original publications were collected from 1993 to 2017. All the articles selected had 3 criteria:

1) Studies on the association between βlg polymorphism and yield traits (for example; lactation milk yield, fat content, protein content, lactose content, casein content),
2) The number of animals and the βlg genotype,
3) The mean of the relevant yield trait of each genotype and the standard deviation or standard error.

**Data extraction:** We extracted the data using a standard form of the content of each study prepared independently of each other in MicroSoft Excel. The content of the studies covered the name of the first author, the date and country of publication, the breed of animals, the number of animals examined, the number of genotypes, the Hardy-Weinberg Equilibrium, the mean of the relevant yield traits of genotypes, the standard deviation of the means and the statistical significance level of the association.

**Statistical analysis:** The data set was prepared separately for each yield trait and the following methods were followed:

i. In the meta-analysis, the analysis of the differences between the means was carried out according to the random effect model or fixed effect model. The model selection is made depending on whether the effects of studies are homogeneous or heterogeneous (Hintze, 2007). Accordingly, the fixed effect model was used when the differences of the means used in the study were homogeneous, and the random effect model was used when they were heterogeneous. The assumption of heterogeneity was calculated based on the $I^2$ statistics (for the significance level of heterogeneity test (p), the level-0.10 was used).

ii. The form of inheritance of the alleles to be used in the study was examined as dominant (AA+AB versus BB), complete over-dominant (AA+BB versus AB), recessive (AA versus AB+BB), co-dominant (AA versus AB, AA versus BB, and AB versus BB) (Ozdemir *et al*., 2018).

iii. In the analysis of the factors, βlg genotype differences on the related yield trait were evaluated according to the breeding, types of the sheep breed (Dairy Subgroup: Dairy sheep breeds and/The Others Subgroup: Dual purpose breeds and various crossbreeds) and were evaluated as overall.

iv. Standard mean differences (SMD) and standard errors were calculated with 95% CI to assess the power of the association between the means of the yield traits of the βlg gene variants examined. This procedure was used to compare all paired (multiply pairwise) variants. In the SMD calculation, the Cohen method (Cohen, 1988) was used when the number of the studies examined was large (>10), and the Hedges method (Hedges, 1981) was used when the number of the studies was low. If the number of studies >10, the Cohen method for standardized mean differences is advantageous. There is an overestimation of the effect size in case of a small number of studies. The Hedges method for standardized mean differences has advantages in the case of a small number of studies (DeCoster, 2004).

v. STATA version 11.0 (Stata Corp. 2009, Stata Statistical Software) was used in all statistical analyses.

**An example for the dataset:** The association among the βlg genotypes and the total milk yield is presented in Table 1, as an example of the dataset utilized in the present study. All the data set used as material in the study can be seen as supplemental files.

## RESULTS AND DISCUSSION

The data set utilized in the present study were organized separately according to economic production traits, loci, and genetic models. Prior to performing the statistical evaluation, the dominant (AA+AB versus BB), complete over-dominant (AA+BB versus AB), recessive (AA versus AB+BB), co-dominant (AA versus AB, AA versus BB and AB versus BB) statuses of the alleles were considered (Table 2). According to the results of the analysis, generally the co-dominant feature as genetic model was displayed, so the association analyzes were performed according to this model.

Tables 2 and 3 contain information on the number of studies and the results of the meta-analysis in which different methods (Cohen or Hedges) were employed depending on the status of whether the studies were homogeneous or heterogeneous. The tables contain information on the Heterogeneity test, SMD, and 95% CI values, its % weight, P values of the pairwise comparisons.

When the genetic model analyses conducted on βlg genotypes and yield traits were examined, it was found out that the genotype mean differences in terms of the total milk yield, fat, protein, and lactose content were not statistically significant in the Dominant and Recessive genetic models, and the mean differences of the fat and casein content were significant only in the Complete over-dominant model and generally AB genotype was determined as superior in the dairy subgroups (Table 2).

In the meta-analysis using 14 studies on the total milk yield, the associations between βlg genotypes (AA vs AB, AA vs BB, and AB vs BB) and the total milk yield were found to be significant in all the sheep and

**Table 1. Studies investigating the association among βlg polymorphism and total milk yield in sheep.**

| First Author | Breeds | N | Country | Type | AA | SD1 | N1 | AB | SD2 | N2 | BB | SD3 | N3 | P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Corral *et al*., 2010 | Merino | 529 | USA | other | 40.24 | 18.71 | 301 | 39.93 | 18.76 | 200 | 47.46 | 19.21 | 28 | |
| Erdogan and Cemal, 2010 | ÇineÇaparı | 40 | Turkey | dairy | 104.69 | 10.61 | 4 | 64.25 | 5.28 | 21 | 76.39 | 5.91 | 15 | * |
| Mroczkowski *et al*., 2004 | Merino | 770 | Poland | other | 30.67 | 11.81 | 193 | 31.03 | 12.60 | 376 | 31.64 | 11.77 | 201 | ns |
| Ramos *et al*., 2009 | Serra da Estrela | 1025 | Portugal | dairy | 118.46 | 58.23 | 406 | 124.31 | 2.82 | 470 | 120.41 | 44.43 | 149 | * |
| Ramos *et al*., 2009 | Merino | 314 | Portugal | other | 77.16 | 25.10 | 66 | 83.15 | 26.88 | 132 | 86.39 | 25.74 | 116 | * |
| Giambra *et al*., 2014 | Lacaune | 749 | Switzerland | dairy | 371.00 | 115.33 | 133 | 372.00 | 118.03 | 387 | 367.00 | 136.19 | 229 | ns |
| Giambra *et al*., 2014 | East Friesian | 394 | Germany | dairy | 284.00 | 107.99 | 238 | 589.00 | 124.90 | 156 | | | | ns |
| Martinez *et al*., 1993 | Manchega | 3672 | Spain | dairy | 58.67 | 4.64 | 1364 | 59.29 | 4.15 | 1748 | 54.96 | 2.36 | 560 | *** |
| Michalcova and Krupova, 2009 | Impr. valachian | 67 | Slovenia | other | 100.50 | 5.28 | 17 | 10.28 | 3.65 | 34 | 102.45 | 4.08 | 16 | ns |
| Michalcova and Krupova, 2009 | Czigaia | 45 | Slovenia | other | 86.56 | 7.56 | 16 | 88.28 | 5.52 | 19 | 97.93 | 7.62 | 10 | ns |
| Esenbuga, 1995 | Morkaraman | 113 | Turkey | other | 73.27 | 35.29 | 20 | 69.75 | 37.65 | 65 | 69.94 | 35.82 | 28 | ns |
| Esenbuga, 1995 | İvesi | 95 | Turkey | dairy | 105.03 | 35.16 | 33 | 114.87 | 36.40 | 53 | 95.66 | 35.10 | 9 | ns |
| Triantaphyllopoulos *et al*.,2017 | Chios and Karag. | 217 | Greece | other | 904.90 | 201.65 | 17 | 1058.34 | 84.26 | 134 | 770.11 | 115.81 | 66 | ns |
| Rozbicka-Wieczorek *et al*.,2015 | Heath and Lowl. | 60 | Poland | other | 37.93 | 13.408 | 10 | 43.44 | 25.44 | 36 | 38.57 | 15.865 | 14 | ns |

*:significant, ns: non-significant, SD: standart deviation, N: sample size

subgroups ($p<0.05$). While the difference between AB vs BB genotypes in the other subgroup was found to be significant ($p<0.05$), the difference between the means of AA vs AB genotypes in the dairy subgroup was found to be significant ($p<0.05$), the difference between the means of AA vs AB and AB vs BB genotypes in the dairy subgroup was found to be significant ($p<0.05$). The differences between the means of the total milk yield of the genotypes in all sheep were found to be insignificant ($p>0.05$). It was determined that the genotypes were ranked as AA>BB>AB in terms of the total milk yield (Table 3). In the individual studies conducted, while some researchers reported that the total milk yield means between βlg genotypes were significant (Martinez *et al*., 1993; Ramos *et al*., 2009), the others reported that the mean differences were insignificant (Mroczkowski *et al*., 2004; Michalcova and Krupova, 2009; Giambra *et al*., 2014; Rozbicka-Wieczorek *et al*., 2015; Triantaphyllopoulos *et al*., 2017).

In the analysis of 21 studies, no significant association was found between βlg genotypes and fat content in all sheep and milk-type sheep group ($P>0.05$). While some researchers reported that the fat content means between βlg genotypes were significant (Dario *et al*., 2008; Ramos *et al*., 2009; Yousefi *et al*., 2013; Giambra *et al*., 2014; Ozmen and Kul, 2016). on the other hand, they reported that the mean differences were insignificant (Esenbuga, 1995; Giaccone *et al*., 2000; Michalcova and Krupova, 2009; Rozbicka-Wieczorek *et al*., 2015; Triantaphyllopoulos *et al*., 2017).

In the analysis of 20 studies, while no significant association was determined between βlg genotypes and the protein content in all sheep ($p>0.05$), in the dairy group, the protein content means of AA vs AB genotypes were found to be statistically different ($p<0.05$) and AB genotype was found to be superior. While there was no statistically significant association between the protein content means of AA vs AB and AA vs BB genotypes in the other subgroup, a significant difference ($p<0.01$) was determined between AB vs BB genotype means and the protein content of BB genotype was found to be superior (Table 3). While some authors reported that the protein content means were significant between βlg genotypes (Mroczkowski *et al*., 2004; Celik and Ozdemir, 2006; Ramos *et al*., 2009; Giambra *et al*., 2014), the othersreported that the mean differences were insignificant (Michalcova and Krupova, 2009; Yousefi *et al*., 2013; Rozbicka-Wieczorek *et al*., 2015; Triantaphyllopoulos *et al*., 2017).

In the analysis of 12 studies used to test the associationbetween βlg genotypes and the lactose content, no significant difference was found between the means in all sheep and other subgroup genotypes in terms of the lactose content ($p>0.05$). While some authors reported in the individual studies conducted that the lactose content means were significant between βlg genotypes and AB genotype was superior (Celik and Ozdemir, 2006; Yousefi *et al*., 2013; Rozbicka-Wieczorek *et al*., 2015; Triantaphyllopoulos *et al*., 2017);the others reported that the mean differences were insignificant (Mroczkowski *et al*., 2004; Michalcova and Krupova, 2009; Ozmen and Kul, 2016).

In the analysis of 5 studies used to test the association between βlg genotypes and the casein content, while there was a statistically significant association($p<0.01$) between AA vs BB genotypes in terms of the casein content in all sheep, the association between AA vs AB and AB vs BB genotype means were found to be insignificant ($p>0.05$). A statistically significant association was determined between the casein content values of all βlg genotypes in the other subgroup, and the ranking of the genotypes was BB>AB>AA (Table 3). No significant relationship was determined between the casein content means of all genotypes in the dairy sub-group ($p>0.05$). While some researchers reported in the individual studies conducted that the casein content means were significant between βlg genotypes (Martinez *et al*., 1993; Rozbicka-Wieczorek *et al*., 2015), the others reported that the mean differences were insignificant (Mele *et al*., 2007; Lupolov and Petcu, 2013).

The results of association studies among βlg polymorphism and economic yield traits are conflicting. These may be due to differences in the sample size, breeds studied, environmental effects, especially genotype-environmental interactions. Breeders should take into account the environmental conditions, animal breeds and genotype-environmental interactions and should use this information for breeding purposes (Supplementary file).

**Conclusion:** The association between βlg gene and certain economic yield traits was investigated and assessed in accordance with a number of genetic models in the meta-analysis. The Meta-analysis shows that the association of βlg gene must generally be investigated in accordance with the co-dominant genetic model. A significant association was found among βlg genotypes and total milk yield, protein content and casein content studied with the meta-analysis. The βlg gene AA genotype for total milk yield, AB genotype for protein content and casein content have significant superiority especially in dairy subgroup, but important candidate genotype for fat content and lactose content could not be determined. It is suggested that βlg major gene will be beneficial for the improvement of the economic yield traits studied, and it is possible to utilize it as major gene and a molecular marker.

**Conflict of Interest:** We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

**Table 2. Genetic model analyses of the genotypes related to βlg.**

| Traits | Type | n | AA+AB versus BB, Dominant Model | | | | | | AA versus AB+BB, Resesive Model | | | | | | AA+BB versus AB, Copmlete over Domn. Model | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | $I^2$ | SMD | 95% | CI | %Weight | P | $I^2$ | SMD | 95% | CI | %Weight | P | $I^2$ | SMD | 95% | CI | %Weight | P |
| Total | Dairy | 6 | 97,7$^{**}$ | 0,146 | -0,442 | 0,734 | 40,84 | 0,626 | 98,8$^{**}$ | -0,012 | -0,683 | 0,659 | 44,50 | 0,972 | 98.6$^{**}$ | -0,256 | -0,815 | 0,304 | 45,52 | 0,370 |
| Milk | Other | 8 | 97,8$^{**}$ | -0,834 | -1,705 | 0,038 | 59,16 | 0,061 | 94,9$^{**}$ | 0,260 | -0,272 | 0,792 | 55,50 | 0,338 | 97.7$^{**}$ | 0,282 | -0,402 | 0,966 | 54,48 | 0,420 |
| Yield | Overall | 14 | 97,9$^{**}$ | -0,245 | -0,722 | 0,232 | 100,00 | 0,313 | 97,6$^{**}$ | 0,101 | -0,290 | 0,492 | 100,00 | 0,613 | 98.1$^{**}$ | -0,075 | -0,464 | 0,315 | 100,00 | 0,708 |
| Fat | Dairy | 9 | 95,9$^{**}$ | -0,244 | -0,945 | 0,457 | 40,36 | 0,495 | 91,0$^{**}$ | -0,235 | -0,509 | 0,038 | 48,37 | 0,092 | 88.8$^{**}$ | -0,22 | -0,438 | -0,003 | 48,06 | **0,047** |
| Content | Other | 11 | 68,8$^{**}$ | 0,101 | -0,105 | 0,307 | 59,64 | 0,336 | 89,9$^{**}$ | 0,075 | -0,262 | 0,411 | 51,63 | 0,664 | 90.4$^{**}$ | 0,553 | 0,249 | 0,857 | 51,94 | **0,000** |
| | Overall | 20 | 91,1$^{**}$ | 0,029 | -0,252 | 0,311 | 100 | 0,838 | 89,9$^{**}$ | -0,063 | -0,257 | 0,130 | 100,00 | 0,521 | 90.0$^{**}$ | 0,141 | -0,032 | 0,314 | 100,00 | 0,109 |
| Protein | Dairy | 8 | 95,9$^{**}$ | -0,244 | -0,945 | 0,457 | 40,36 | 0,495 | 88,3$^{**}$ | -0,005 | -0,327 | 0,317 | 44,06 | 0,977 | 90.4$^{**}$ | 0,015 | -0,298 | 0,327 | 43,73 | 0,926 |
| Content | Other | 11 | 68,8$^{**}$ | 0,101 | -0,105 | 0,307 | 59,64 | 0,336 | 92,1$^{**}$ | 0,245 | -0,120 | 0,609 | 55,94 | 0,188 | 95.0$^{**}$ | 0,100 | -0,299 | 0,499 | 56,27 | 0,622 |
| | Overall | 19 | 91,1$^{**}$ | 0,029 | -0,252 | 0,311 | 100,00 | 0,838 | 90,5$^{**}$ | 0,134 | -0,104 | 0,372 | 100,00 | 0,269 | 93.5$^{**}$ | 0,068 | -0,182 | 0,317 | 100,00 | 0,594 |
| Lactose | Dairy | 2 | 99,0$^{**}$ | 3,192 | -2,913 | 9,297 | 17,15 | 0,305 | 98,6$^{**}$ | 1,457 | -1,465 | 4,379 | 17,35 | 0,328 | 0,0 | -0,099 | -0,334 | 0,136 | 17,44 | 0,411 |
| Content | Other | 9 | 95,9$^{**}$ | -0,348 | -0,990 | 0,294 | 82,85 | 0,288 | 93,2$^{**}$ | -0,269 | -0,699 | 0,162 | 82,65 | 0,221 | 96.1$^{**}$ | -0,373 | -0,875 | 0,128 | 82,56 | 0,145 |
| | Overall | 11 | 96,8$^{**}$ | 0,197 | -0,490 | 0,883 | 100,00 | 0,574 | 94,9$^{**}$ | -0,026 | -0,480 | 0,428 | 100,00 | 0,911 | 95.3$^{**}$ | -0,328 | -0,745 | 0,089 | 100,00 | 0,124 |
| Casein | Dairy | 4 | 76,3$^{**}$ | 0,27 | -0,132 | 0,673 | 83,84 | 0,188 | 27,6 | -0,076 | -0,224 | 0,073 | 85,74 | 0,318 | 0,0 | -0,266 | -0,328 | -0,204 | 83,50 | **0,000** |
| Content | Other | 1 | 0,0 | -6,612 | -7,974 | -5,25 | 16,16 | **0,000** | 0,0 | -3,816 | -4,795 | -2,836 | 14,26 | **0,000** | 0,0 | 2,932 | 2,183 | 3,682 | 16,50 | **0,000** |
| | Overall | 5 | 96,5$^{**}$ | -0,84 | -1,876 | 0,196 | 100,00 | 0,112 | 93,5$^{**}$ | -0,645 | -1,227 | -0,062 | 100,00 | **0,030** | 94.3$^{**}$ | 0,311 | -0,255 | 0,878 | 100,00 | 0,281 |

(for $I^2$; $^{*}$:P<0.10 $^{**}$:P<0.01), n:number of publication

**Table 3. The results of the Meta-analysis regarding the association between βlg genotypes and certain yield traits; SMD values and certain statistical results.**

| Traits | Type | n | AA versus AB | | | | | | AA versus BB | | | | | | AB versus BB | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | $I^2$ | SMD | 95% | CI | %Weight | P | $I^2$ | SMD | 95% | CI | %Weight | P | $I^2$ | SMD | 95% | CI | %Weight | P |
| Total | Dairy | 6 | 19,2 | 1,419 | 0,214 | 2,624 | 36,66 | **0,021** | 82,3$^{**}$ | 0,183 | -0,257 | 0,623 | 35,560 | 0,415 | 96,8$^{**}$ | -1,07 | -1,983 | -0,157 | 33,08 | **0,022** |
| Milk | Other | 8 | 98,8$^{**}$ | -0,109 | -0,198 | -0,021 | 63,34 | **0,016** | 95,8$^{**}$ | -0,078 | -0,607 | 0,452 | 64,440 | 0,774 | 97,3$^{**}$ | 0,072 | -0,484 | 0,628 | 66,92 | 0,800 |
| Yield | Overall | 14 | 97,2$^{**}$ | -0,051 | -0,434 | 0,332 | 100,00 | 0,795 | 94,8$^{**}$ | 0,07 | -0,304 | 0,444 | 100,00 | 0,714 | 97,4$^{**}$ | -0,254 | -0,718 | 0,209 | 100,00 | 0,282 |
| Fat | Dairy | 9 | 83,0$^{**}$ | 0,033 | -0,247 | 0,313 | 44,87 | 0,818 | 90,6$^{**}$ | -0,081 | -0,677 | 0,515 | 40,73 | 0,790 | 94,0$^{**}$ | -0,06 | -0,674 | 0,553 | 41,02 | 0,847 |
| Content | Other | 12 | 92,3$^{**}$ | 0,245 | -0,152 | 0,642 | 55,13 | 0,226 | 74,7$^{**}$ | -0,003 | -0,293 | 0,288 | 59,27 | 0,986 | 90,4$^{**}$ | 0,21 | -0,180 | 0,601 | 58,98 | 0,291 |
| | Overall | 21 | 89,7$^{**}$ | 0,159 | -0,083 | 0,401 | 100,00 | 0,197 | 84,3$^{**}$ | -0,004 | -0,280 | 0,271 | 100,00 | 0,975 | 91,9$^{**}$ | 0,12 | -0,194 | 0,434 | 100,00 | 0,452 |
| Protein | Dairy | 9 | 91,8$^{**}$ | -0,321 | -0,621 | -0,021 | 48,70 | **0,036** | 84,2$^{**}$ | -0,031 | -0,348 | 0,287 | 48,73 | 0,850 | 81,0$^{**}$ | 0,21 | -0,036 | 0,456 | 47,17 | 0,095 |
| Content | Other | 11 | 85,4$^{**}$ | 0,288 | -0,014 | 0,591 | 51,30 | 0,062 | 91,2$^{**}$ | -0,242 | -0,784 | 0,300 | 51,27 | 0,381 | 93,1$^{**}$ | -0,748 | -1,250 | -0,247 | 52,83 | **0,003** |
| | Overall | 20 | 88,7$^{**}$ | -0,006 | -0,200 | 0,188 | 100,00 | 0,952 | 90,0$^{**}$ | -0,07 | -0,358 | 0,218 | 100,00 | 0,635 | 91,8$^{**}$ | -0,18 | -0,448 | 0,088 | 100,00 | 0,188 |
| Lactose | Dairy | 2 | 97,9$^{**}$ | 1,097 | -1,160 | 3,354 | 17,96 | 0,341 | 98,2$^{**}$ | 3,002 | -2,814 | 8,818 | 17,14 | 0,312 | 98,4$^{**}$ | 2,713 | -2,424 | 7,850 | 17,16 | 0,301 |
| Content | Other | 10 | 93,1$^{**}$ | -0,382 | -0,846 | 0,083 | 82,04 | 0,107 | 89,6$^{**}$ | -0,362 | -0,898 | 0,173 | 82,86 | 0,185 | 95,8$^{**}$ | -0,039 | -0,716 | 0,638 | 82,84 | 0,911 |
| | Overall | 12 | 94,2$^{**}$ | -0,142 | -0,598 | 0,314 | 100,00 | 0,542 | 92,8$^{**}$ | 0,028 | -0,568 | 0,625 | 100,00 | 0,926 | 96,2$^{**}$ | 0,381 | -0,295 | 1,058 | 100,00 | 0,269 |
| Casein | Dairy | 4 | 0,0 | -0,151 | -0,219 | -0,084 | 88,09 | **0,000** | 73,2$^{*}$ | 0,167 | -0,263 | 0,597 | 95,92 | 0,447 | 78,9$^{**}$ | 0,33 | -0,115 | 0,775 | 84,19 | 0,146 |
| Content | Other | 1 | 0,0 | -2,109 | -2,942 | -1,276 | 11,91 | **0,000** | 0,0 | -12,55 | -16,520 | -8,584 | 4,08 | **0,000** | 0,0 | -6,279 | -7,702 | -4,856 | 15,81 | **0,000** |
| | Overall | 5 | 82,1$^{**}$ | -0,429 | -0,804 | -0,055 | 100 | **0,025** | 92,3$^{**}$ | -0,361 | -1,230 | 0,508 | 100,00 | 0,415 | 96,1$^{**}$ | -0,721 | -1,743 | 0,301 | 100,00 | 0,167 |

(for $I^2$; $^{*}$:P<0.10 $^{**}$:P<0.01), n:number of publication

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