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Investigation of the Use of Phytase Enzyme as a Feed Additive in the Nutrition of Broiler Chicks by Meta Analysis

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ABSTRACT

In this study, it was aimed to combine the results obtained from independent studies conducted between 1999 and 2019 on the use of phytase enzyme in the feeding of broiler chickens with meta-analysis and to reach a general conclusion. The criteria by which the studies to be included in the meta-analysis were brought together were determined within the framework of certain criteria. At the end of these criteria, the quantitative data of the studies discussed were brought together and interpreted using the analysis method in the Meta-Essentials Excel Program. It is understood from the values of I^2 = 0.00% that there is no heterogeneity in all parameters (LW, FCR, FI, DLWG, bone Ca and P content) examined in broiler chickens. It is seen as a result of the calculated P (0.953, 0.955, 0.939) values that the subgroups created from the publications used are not different from each other. Because of the trend analysis (Q = 0.06, 0.15, 0.13), it was understood that there was no heterogeneity and no significant deviation. This situation is supported by the results obtained with the Khi- square analysis (0.752, 0.697, 0.752). As a result of the moderator analysis, no difference was found in R^2 (33.88%, 0.38%, 14.25%) and P (0.047, 0.849, 0.226) values. To conclude, the heterogeneity, subgroup, moderator, trend and Failsafe N test analyzes performed with meta analysis showed that the effects of phytase enzyme on live weight, live weight gain, feed consumption and feed conversion ratio parameters were similar to each other.

Meta Analizi İle Fitaz Enziminin Yem Katkı Maddesi Olarak Etlik Civcivlerin Beslenmesinde Kullanımının Araştırılması

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ÖZET

Bu çalışmada, 1999-2019 yılları arasında etlik civcivlerin beslenmesinde fitaz enzimi kullanımı ile ilgili yapılmış birbirinden bağımsız çalışmalardan elde edilen sonuçların meta analiz ile birleştirilmesi ve genel bir yargıya varılması amaçlanmıştır. Meta analizine dahil edilecek araştırmaların hangi kriterlere göre bir araya getirileceği belli ölçütler çerçevesinde gerçekleştirilmiştir. Bu ölçütler sonunda ele alınan çalışmaların nicel verileri bir araya getirilerek yorumlanması Meta-Essentials Excell Programındaki analiz yöntemiyle sağlanmıştır. Etlik civcivlerde incelenen parametrelerin (CA, YDO, YT, GCAA, kemik Ca ve P içeriği) tümünde heterojenitenin olmadığı, I^2= %0,00 değerlerinden anlaşılmaktadır. Kullanılan yayınlardan oluşturulan alt grupların da birbirinden farklı olmadığı hesaplanan P (0.953, 0.955, 0.939) değerleri sonucunda görülmektedir. Eğilim analiz sonucunda ise (Q=0,06, 0,15, 0,13) heterojenite ve herhangi önemli bir sapmanın olmadığı anlaşılmıştır. Bu durumu Khi-kare analizi ile elde edilen sonuçlar (0.752, 0.697, 0.752) desteklemektedir. Moderatör analiz sonucunda ise R^2 (%33.88, %0.38, %14.25) ve P (0.047, 0.849, 0.226) değerlerinde farklılık bulunmamıştır. Sonuç olarak, meta analizi ile yapılan heterojenite, alt grup, moderatör, eğilim ve Failsafe N testi analizleri fitaz enziminin canlı ağırlık, canlı ağırlık artışı, yem tüketimi ve yem dönüşüm oranı parametrelerine olan etkisinin birbirine benzer olduğu göstermiştir.

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1. INTRODUCTION

Phytases are phosphatase enzymes that hydrolyze phosphate ester bonds and have a molecular weight ranging from 1.6 to 1.8 x 105 Da, and they have a glycoprotein structure (Özkan, 2009). Abbreviations such as FTU, FYT, PU and U are used to describe phytase activity. As a result of the effects of the phytase enzyme on the phytate molecule, the utilization of minerals taken with the diet increases significantly, therefore the phytase enzyme is important in terms of nutrition (Tatlı, 2007).

Huff et al. (1998) reported that adding phytase to broiler chick rations based on high phosphorus corn increased live weight (LW) but had no significant effect on feed conversion ratio (FCR). They also reported that when phytase was supplemented in diets prepared with high phosphorus corn, total phosphorus could be reduced by at least 25% without affecting the performance or health of the chicks.

Kocabağlı (2001) investigated the effect of phytase addition to a corn and soybean meal-based diet on P and Ca availability in broiler chickens. As a result of the experiment, it was emphasized that the addition of phytase increased the tibia ash ratio, tibia fracture resistance and flexibility, but increasing the phytase dose from 300 U/kg to 700 U/kg did not provide any additional benefit on tibiotarsal bone properties and durability in broiler chickens.

Lan et al. (2002) investigated the effect of phytase supplementation in corn-soy-based diets on growth performance in broiler chickens. As a result, they determined that phytase supplementation to low NPP diet increased growth performance, AME value, digestibility of CP and DM, Ca, P and Cu utilization and bone mineralization.

Ahmed et al. (2004) investigated the effects of different amounts of phytase supplementation in the soy-based diet of broiler chickens on performance in a 21-day trial. They reported that as the dose of phytase increased, feed consumption and live weight gain increased, but it had no effect on mortality.

Singh and Khatta (2004) conducted a 6-week study to determine the effects of phytase supplementation on growth performance and economy in broiler chicken production. They found that phytase supplementation to high non-phytate phosphorus (NPP) diets increased growth performance, reduced feed costs, and made broiler chicken production economical in terms of weight gain. They reported that phytase supplementation was more effective in corn-based rations.

Yardibi (2005) found that phytase supplementation improved feed utilization and bone fracture resistance in broiler chickens.

Akyürek et al. (2005) found that phytase added to the rations of broiler chickens increased live weight. They reported that it provided a significant increase in Ca and P availability and a significant decrease in the amount of Ca and P excreted in feces.

Çimrin (2006) reported that phytase addition to low-phosphorus broiler chicken diets had a positive effect on live weight, live weight gain and carcass weight, and also did not affect serum phosphorus levels.

Karimi (2006) reported that phytase supplementation in broiler chicken diets containing usable P at two different levels 0 and 500 F.T.U/kg. In his study examining the effect on performance between days, all groups 0-20. It was reported that the productivity parameters (live weight, feed consumption and feed conversion ratio) between days were not affected by the phytase enzyme supplement, and feed intake was significantly increased only at the age of 21-40 days.

Bingöl et al. (2009) reported that broiler chickens fed a low-phosphorus diet supplemented with phytase increased body weight and serum P levels and reduced the amount of P excreted in feces. They concluded that with the addition of 1000 g phytase/tone in the diet of broiler chickens, dietary phosphorus can be reduced by up to 30% without affecting animal performance.

Ceylan et al. (2012) stated that phytase supplementation added to broiler chick diets containing four different levels of phosphorus increased growth performance and significantly reduced the phosphorus level in feces, and the total phosphorus level in broiler chick diets could be reduced by 0.13%.

Chen et al. (2013) reported that phytase supplementation could increase the growth performance of broiler chickens.

Abdel Megeed and Tahir (2015) reported that the addition of phytase to broiler chick diets significantly increased body weight gain (BWG) and feed intake (FI), and also significantly reduced the P and Ca levels in feces.

Süzer et al. (2015) found that the use of phytase as a feed additive increased the 42-day growth performance of broiler chickens.

Ahmed et al. (2015) stated that the addition of 500 FTU/kg phytase to broiler chickens fed with diets containing low levels of P improved growth performance, carcass weight and bone mineralization.

Süzer (2016) reported that phytase supplementation to the diets of broiler chickens increased bone mineral content, biomechanical properties and durability of broiler chickens.

Meta analysis literally means "advanced, beyond" and has been defined by many researchers as "analysis of analyses" (Kurt, 2009). Meta analysis is a statistical method that helps to combine qualitatively and quantitatively the results of research conducted in different places, times and centers on the same subject and to reach a general conclusion on that subject. The specific aspect of the analysis is that it uses quantitative methods rather than relying on judgment alone. The meta-analysis method is a quantitative study method, unlike other literature review methods, as it is based on statistical techniques and numerical data (Demiray, 2013). By combining the results obtained from different studies on a similar problem with meta analysis, increasing the sample size and thus making stronger and more precise parameter estimates for the problem, improving the effect size estimates, investigating the heterogeneity between studies and determining the factors that cause this heterogeneity, if any, possible studies. It is possible to prevent bias, evaluate the inconsistencies in studies and examine their reasons, find answers to questions that were not considered at the beginning of the study, reach a general conclusion on the subject under investigation, and help future research and decisions to be made (Şelli, 2011; Demirel, 2005). The results of the meta-analysis reflect the analyzed literature and the limits of this literature (Demiray, 2013).

It was reported that in scientific research, with meta-analysis, the validity of individual studies with similar findings can be tested and strengthened, and it is possible to see the reasons for the differences in individual studies with different findings. It was stated that from this perspective, the issue can be followed in more detail and new hypotheses can be established and analyzed (Şelli and Doğan, 2011).

In meta-analysis, unlike classical and systematic review studies, the results obtained from different studies are evaluated statistically together and more general conclusions are tried to be drawn. In this respect, meta analysis is a statistical analysis method that is needed in many branches of science and enables general evaluation (Karahan, 2010).

As an example of a meta-analysis study, Bougouin et al. (2014) quantitatively summarized the effect of phytase on phosphorus accumulation in broiler and layer chickens. They included data from 103 and 26 controlled trials testing the effect of phytase on phosphorus accumulation in 2 separate meta-analyses for broiler and laying hens, respectively. In their results, they reported that there was a significant positive effect on phosphorus accumulation in both broiler and laying hens, but the effect sizes between studies were significantly heterogeneous due to differences in Ca contents, trial period, animal age and phytase dose. In our country, studies of this nature are quite limited. Therefore, the aim of this study was to obtain a more precise understanding of the subject by utilizing the results of research conducted on the effect of phytase enzyme supplementation in broiler chicken feeding on LW, DLWG, FI, FCR, bone Ca and P content and combining these findings with meta-analysis, one of the statistical methods. to obtain judgment and to shed light on future studies on this subject.

2. MATERIAL AND METHODS

In this study, the meta-analysis method, which is considered systematic synthesis, was used. This meta-analysis study consists of statistical synthesis and interpretation of the quantitative findings of independent studies.

In determining the study, research articles, master's and doctoral theses were scanned in search engines on the internet (Medline, Google Scholar, Pubmed, Web of Science) with the keywords "phytase + poultry + broiler + laying hens + quail". In this context, 441 studies were scanned, but some were qualitative studies, some studies did not have control groups or were missing in terms of the parameters taken into account (LW-FCR, FI-DLWG, bone Ca-P content). Therefore, 46 studies that were most suitable for meta-analysis were selected. Since some publications were used repeatedly in different parameters, 36 publications were subjected to a meta-analysis (Van Rhee et al. 2018). Only the broiler chicks section (LW: Live weight, FI; Feed intake, DLWG: Daily live weight gain, FCR: Feed conversion ratio, bone Ca and P content) from the thesis study is written here.

Table 1. Data inputs regarding final live weight and feed conversion ratio for broiler chicks

No	Studies	a	b	c	d	n1	n2	Sub-group	Moderator
1	Ahmed et al. (2004)	1700	2	1815	2	36	36	AA	15
2	Boney and Moritz (2017)	1389	2	1386	2	290	290	AA	16
3	Broch et al. (2018)	2415	2	2602	2	184	184	AA	13
4	Campasino et al.(2014)	2951	2	3299	2	200	200	AA	18
5	Cerera and Cerera (2014)	1118	2	1203	2	45	45	BB	20
6	Ceylan et al. (2012)	2001	1	2204	1	60	60	BB	14
7	Chen et al. (2013)	2683	2	2830	2	120	120	AA	19
8	Cowieson and Adeola (2005)	878	2	1015	2	144	144	AA	13
9	Abdollahi et al. (2016)	1045	1	1075	1	48	48	BB	19
10	Yan et al. (2004)	3036	2	3000	2	300	300	AA	22
11	Zaefarian et al. (2015)	2125	1	2097	1	48	48	BB	17
12	Zanella et al. (1999)	2650	2	2700	2	240	240	BB	18

In this study, data entries for two groups (control and phytase group) and two parameters each were made using the Meta Essentials package program (Version 1.4) (Van Rhee et al., 2018).

The data were coded in the Meta Essentials package program as the author's name and study year, parameter values of the compared groups (a, b, c, d), number of animals in the control and phytase groups (n1 and n2). The negative control groups in the studies were compared as "Group 1: Control Group" and the groups representing the highest dose of phytase enzyme as "Group 2: Phytase Group" (Table 1).

Three different analyzes were performed on broiler chickens. The parameters evaluated are live weight, feed conversion ratio, feed consumption, daily live weight gain and bone Ca and P content content. These parameters are divided into binary groups to be coded in the Meta Essentials package program. These; LW-FCR, FI-DLWG, bone Ca content-bone P content. Hak et al.(2018), who supported the same package program in interpreting the results. In order to combine the research results appropriately and reach definitive decisions, Combining Effect Sizes of Experimental Studies, one of the Meta-Analysis procedures, and Mantel-Haenszel Fixed Effect Model, DerSimonian-Laird Random Effect Model and Peto Methods Odds Ratio estimates, one of the Meta-Analytical Methods, were used. Chi-Square ($\chi 2$) test statistics and I^2 measurements were used to find heterogeneity. In order to demonstrate the reliability of the meta-analysis results and to reveal publication bias, the 'Number of Studies Increasing the

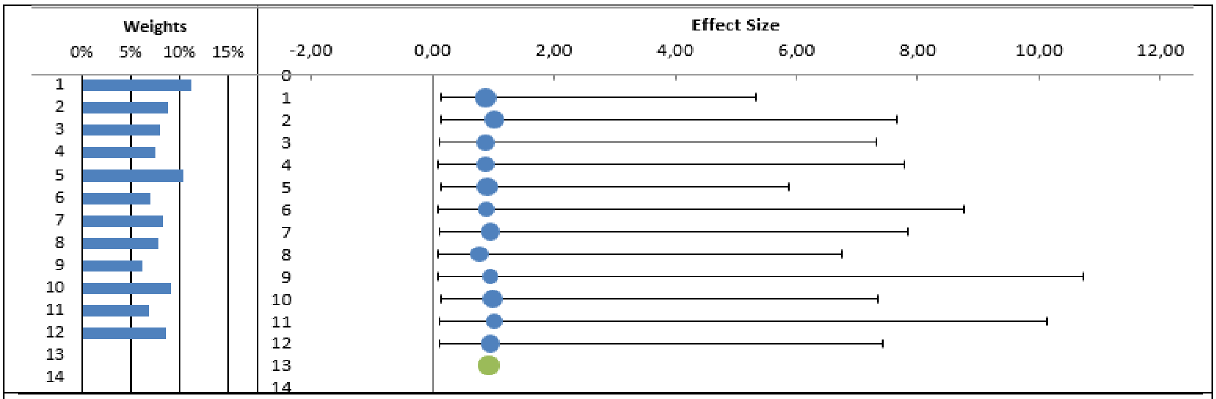
Probability of Confidence (Failsafe N)' was examined and Funnel graphs were evaluated. The statistical calculations used in this study were made with the "Meta Essentials (Version 1.4)" program.

3. RESULTS AND DISCUSSION

The data in the considered publications were analyzed as separate sets in the meta-analysis program, and the secondary data obtained in the meta-analysis are presented in this section.

3.1. Final Live Weight and Feed Conversion Ratio

The result of the data analysis (Forest plot) made by taking into account the control and effective phytase dose of 12 publications studied in different centers between 1999 and 2019, where final live weight and feed conversion ratio were considered together as parameters, is given in detail in Figure 1 below. Figure 1 shows the meta-analysis diagram (Forest plot) in which the effect widths of the studies included in the meta-analysis are given. According to this diagram, it is seen that the effect width of the 12 studies is on the same values when looking at the Odds Ratio values stated both in point and numerical terms, and all 12 studies contribute to the combined result of the meta-analysis. The study that contributed the most to the overall result was the study by Ahmed et al. (2004) with a weight ratio of 11.19%. This study is followed by the study by Cerera and Cerera (2014) with the closest weight ratio (10.44%).



No	Studies	Odds ratio	CI LL	CI UL	Weight %
1	**Ahmed et al.(2004)**	**0.88**	**0.15**	**5.33**	**11.19**
2	Boney and Moritz (2017)	1.01	0.13	7.66	8.87
3	Broch et al.(2018)	0.87	0.10	7.31	8.03
4	Campasino et al.(2014)	0.87	0.10	7.78	7.56
5	**Cerera and Cerera (2014)**	**0.91**	**0.14**	**5.86**	**10.44**
6	Ceylan et al. (2012)	0.90	0.09	8.76	6.98
7	Chen et al. (2013)	0.96	0.12	7.82	8.28
8	Cowieson and Adeola (2005)	0.78	0.09	6.76	7.79
9	Abdollahi et al. (2016)	0.96	0.09	10.73	6.22
10	**Yan et al.(2004)**	**0.99**	**0.13**	**7.35**	**9.06**
11	Zaefarian et al. (2015)	1.02	0.10	10.13	6.90
12	Zanella et al. (1999)	0.96	0.12	7.42	8.68

Figure 1. Effect size for live weight and feed conversion ratio in broiler chickens

Effect sizes are depicted with a circle (●) and the longer the horizontal lines passing through each circle, the wider the confidence interval is. According to Figure 1, the widest confidence interval appears to be the study conducted by Yan et al. (2004). Additionally, 12 of the 12 studies used in the research appear to have a positive effect width. The positive effect width indicates that the effect width is in favor of the experimental group. In addition, the fact that the effect width is greater than zero shows that the effect of phytase enzyme contribution on both parameters (LW and FCR) is statistically significant and positive.

Table 2 shows the combined effect width and heterogeneity analysis results for live weight and feed conversion ratio in broiler chickens. As a result of the analysis, the Odds Ratio value obtained by combining the results of 12 studies was found to be 0.92 (95%: 0.88 - 0.97). Figure 1 and Table 2 show that the relationship between live weight and feed conversion ratio is important because the Z value is less than 1 (-3.61) and the P value is 0.000, and the effects of the phytase enzyme on these parameters are similar due to the I^2 value of 0.00%.

Table 2. Combined effect size and heterogeneity for live weight and feed conversion ratio in broiler chickens

Combined effect size	**Values**
Odds Ratio	0.92
CI Lower limit	0.88
CI Upper limit	0.97
PI Lower limit	0.88
PI Upper limit	0.97
Z-value	-3.61
One-tailed p-value	0.000
Two-tailed p-value	0.000
Number of incl. subjects	49258
Number of incl. studies	12
Heterogeneity	
Q	0.06
P_Q	1.000
I^2	%0.00
T^2 (Odds Ratio)	0.00
T (Odds Ratio)	0.00

The I^2 value is the percentage value showing that the variance between studies is due to heterogeneity rather than chance. The I^2 value being 0.00% shows that there is no heterogeneity and the effects of the phytase enzyme on the examined parameters (LW and FCR) are similar.

Table 3. Analysis of variance for subgroups for live weight and feed conversion ratio in broiler chickens

Analysis of variance	**Sum of squares (Q)**	**df**	**P values**
Between / Model	0.00	1	0.953
Within / Residual	0.05	10	1.000
Total	0.06	11	1.000
Pseudo R^2	%6.12		

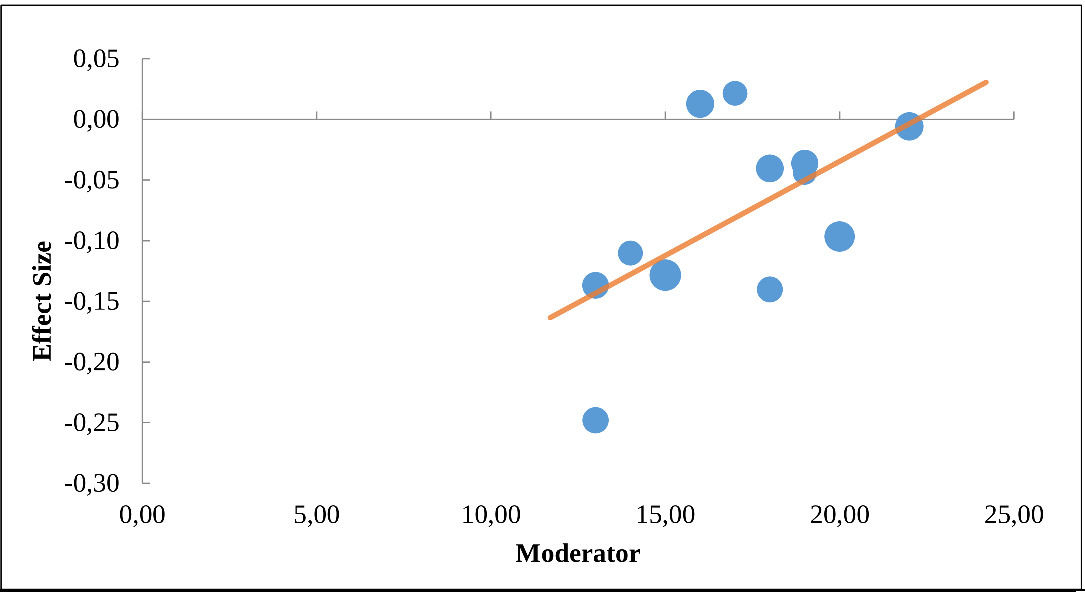
df:degree of freedom

Table 4. Subgroup analysis for live weight and feed conversion ratio in broiler chickens

No	**Subgroups**	**Odds ratio**	**CI LL**	**CI UL**	**Weight %**	**Q**	**P_Q**	**I^2 %**	**T^2**	**T**
1	Ahmed et al. (2004)	0.88	0.15	5.33	18.41					
2	Boney and Moritz (2017)	1.01	0.13	7.66	14.59					
3	Broch et al. (2018)	0.87	0.10	7.31	13.22					
4	Campasino et al. (2014)	0.87	0.10	7.78	12.44					
5	Chen et al. (2013)	0.96	0.12	7.82	13.62					
6	Cowieson and Adeola (2005)	0.78	0.09	6.76	12.82					
7	Yan et al.(2004)	0.99	0.13	7.35	14.91					
8	**AA**	**0.91**	**0.84**	**0.99**	**30.81**	**0.05**	**1.0**	**0.0**	**0.0**	**0.0**
9	Cerera and Cerera (2014)	0.91	0.14	5.86	26.61					
10	Ceylan et al. (2012)	0.90	0.09	8.76	17.81					
11	Abdollahi et al. (2016)	0.96	0.09	10.73	15.85					
12	Zaefarian et al. (2015)	1.02	0.10	10.13	17.59					
13	Zanella et al. (1999)	0.96	0.12	7.42	22.14					
14	**BB**	**0.94**	**0.89**	**1.01**	**69.19**	**0.01**	**1.0**	**0.0**	**0.0**	**0.0**
15	**Combined Effect Size**	**0.93**	**0.90**	**0.97**		**0.06**	**1.0**	**0.0**	**0.0**	**0.0**

When the studies are divided into two groups; The similarity between the results is clearly evident in the analysis of variance in Table 3 and the subgroup analysis in Table 4. From these tables, it can be easily understood that when the studies are divided into two groups (AA and BB) according to the data entry order, there is no difference between the publications in terms of being affected by the phytase enzyme (P = 0.953).

According to Figure 2 below, the regression between LW and FCR (33.88%) was found to be significant (P = 0.047). However, moderator analysis revealed that both parameters were similarly affected by the phytase enzyme contribution (P = 0.889).

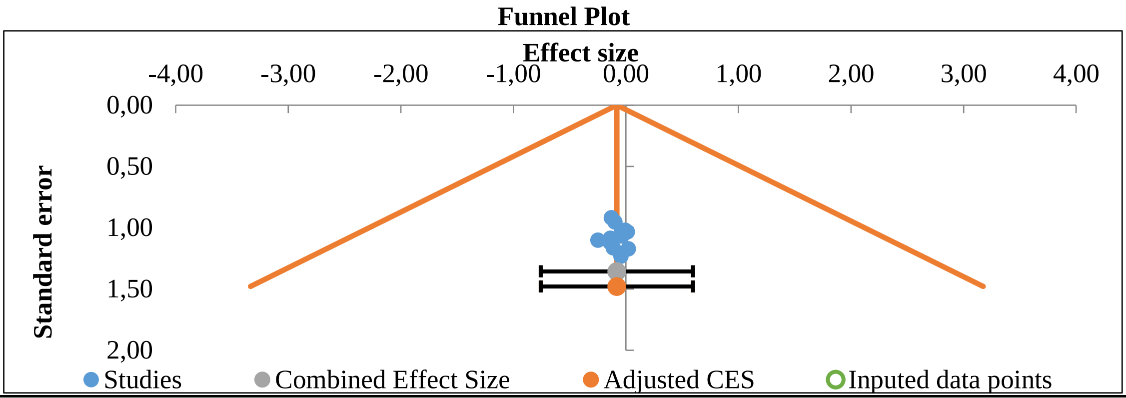


	B	SE	CI LL	CI UL	β	Z-value	P-value
Intercept	-0.35	1.92	-4.58	3.88		-0.18	0.857
Moderator	0.02	0.11	-0.23	0.26	0.58	0.14	0.889

Analysis of variance	**Q**	**DF**	**P**	**Mean square**	**F-Value**	**P-value**
Model	0.02	1	0.889	0.02	5.12	0.047
Residual	0.04	10	1.000	0.00		
Total	0.06	11	1.000			
Combined effect size	-0.08					
T^2	0.00					
R^2	%33.88					

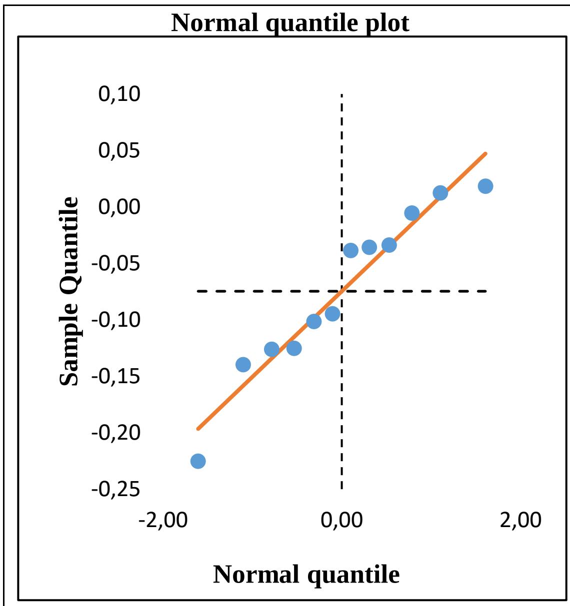
Figure 2. Moderator analysis for live weight and feed conversion ratio in broiler chickens

Each point in Figure 3 represents a separate study. The effect sizes obtained from the studies are on the horizontal axis, and the standard errors obtained from the effect size calculations are on the vertical axis. In the figure, the symmetry axis (vertical line in the middle) in the funnel plot gives the distribution of effect sizes calculated from the studies. Studies distributed evenly (symmetrically) to the right and left of the symmetry axis show that there is no publication bias. The effect width distribution on the Y axis of the Funnel Plot in the figure shows that the I^2 value given for heterogeneity at the bottom of the figure is 0.00%, the tau-square (T^2) value is 0.00 and the PQ value of the Cochran Q statistic is 1.000. This supports the absence of heterogeneity between studies.



Combined effect size	Observed	Combined effect size	Adjusted	Heterogeneity	
Log OR	-0.08	**Log OR**	-0.08	**Q**	0.06
SE Log OR	0.31	**SE Log OR**	0.31	**P_Q**	1.000
CI LL	-0.76	**CI LL**	-0.76	**I^2**	0.00%
CI UL	0.60	**CI UP**	0.60	**T^2**	0.00
PI LL	-0.76	**PI LL**	-0.76	**T**	0.00
PI UL	0.60	**PI UL**	0.60		

Figure 3. Trend analysis for live weight and feed conversion ratio in broiler chickens



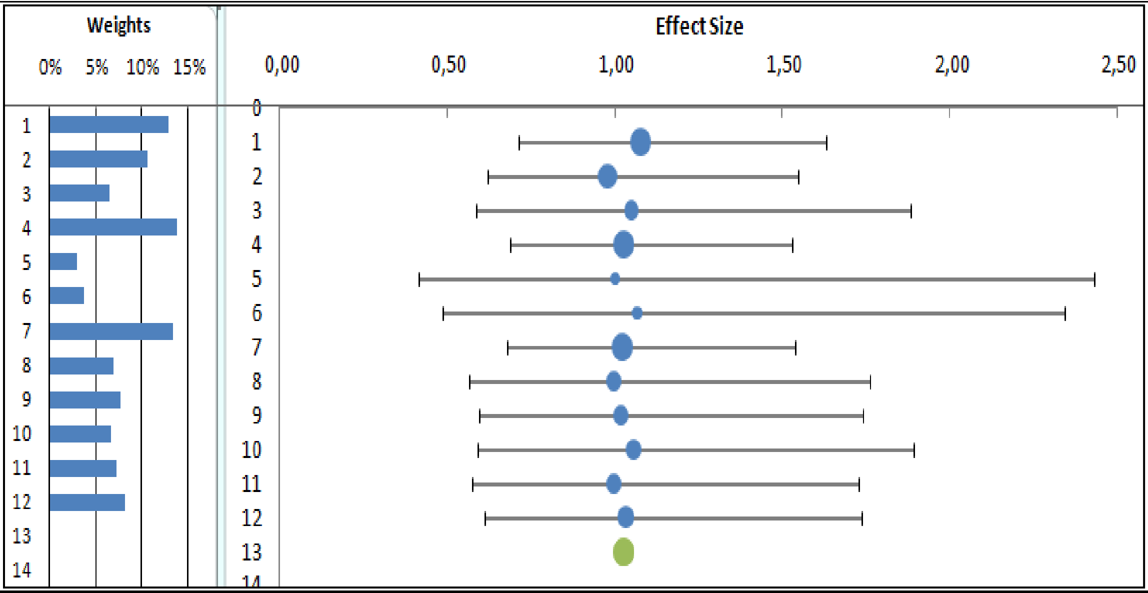
Failsafe N tests	
Rosenthal	
Overall Z-score	-0.26
Failsafe-N	0
Ad-hoc rule	Doğru
Gleser and Olkin	
Number of unpublished studies	11
Orwin	
Combined effect size	-0.08
Criterion value d_C	0
Mean fail safe studies d_{FS}	-0.69
Failsafe-N	0
Fisher	
Failsafe-N	19
p(Chi-square test)	0.752

Figure 4. Failsafe N analysis for live weight and feed conversion ratio in broiler chickens

According to the Failsafe N test, the general Z value is -0.26, the Failsafe -N value is 0, the dc value is 0 and the Chi-square is insignificant, proving that the effect of the phytase enzyme on both parameters (LW and FCR) is the same. Failsafe-N analysis (0) shows that among the 12 studies coded into the meta-analysis program, no study was found that increased the P value, that is, opposed to the effect of the phytase enzyme (Figure 4).

3.2. Feed Intake and Daily Live Weight Gain

The result of the data analysis (Forest plot) made by taking into account the control and effective phytase dose of 12 publications studied in different centers between 1999 and 2019, where feed consumption and daily live weight gain (DLWG) were considered together as parameters, is given in detail in Figure 5 below.



No	Studies	Odds Ratio	CI LL	CI UL	Weight %
1	Zeller et al. (2015)	1.08	0.71	1.63	12.88
2	Akter et al. (2016)	0.98	0.62	1.55	10.53
3	Amerah et al. (2014)	1.05	0.59	1.88	6.50
4	**Han et al. (2009)**	**1.03**	**0.69**	**1.53**	**13.83**
5	Khan et al. (2019)	1.00	0.41	2.43	2.86
6	Olukosi and Adeola (2008)	1.07	0.48	2.34	3.61
7	Saçaklı et al. (2015)	1.02	0.68	1.54	13.31
8	Lim et al. (2001)	1.00	0.57	1.76	6.86
9	Dos Santos et al. (2013)	1.02	0.59	1.74	7.66
10	Swiatkiewicz et al. (2001)	1.06	0.59	1.89	6.52
11	Karimi (2006)	1.00	0.57	1.73	7.27
12	Lü et al. (2009)	1.03	0.61	1.74	8.15

Figure 5. Effect size for feed intake and daily live weight gain in broiler chickens

Figure 5 above shows the meta-analysis diagram (Forest plot) in which the effect widths of the studies included in the meta-analysis are given. According to this diagram, it is seen that the effect width of the 12 studies is on the same values when looking at the OR values stated both in point and numerical terms, and all 12 studies contribute to the combined result of the meta-analysis. The study that contributed the most to the overall result was Han et al.(2009) with a weight ratio of 13.83%. This study has the closest weight ratio (13.31%) to Saçaklı et al. (2015).

According to Figure 5, the widest confidence interval is from Khan et al. (2019)'s study. In addition, it is seen that 12 of the 12 studies used in the research have a positive effect width. The positive effect width indicates that the effect width is in favor of the experimental group. In addition, the fact that the effect width is greater than zero shows that the effect of phytase enzyme coefficient on both parameters (FI and DLWG) is statistically significant and positive.

Table 5. Combined effect size and heterogeneity for feed intake and daily live weight gain in broiler chicks

Combined effect size	Values
Odds Ratio	1.03
CI Lower limit	1.01
CI Upper limit	1.05
PI Lower limit	1.01
PI Upper limit	1.05
Z-value	3.05
One-tailed p-value	0.001
Two-tailed p-value	0.002
Number of incl. subjects	3017
Number of incl. studies	12
Heterogeneity	
Q	0.15
P_Q	1.000
I^2	0.00 %
T^2 (Odds Ratio)	0.00
T (Odds Ratio)	0.00

Table 5 shows the combined effect width and heterogeneity analysis results for feed consumption and daily live weight in broiler chickens. The OR value obtained by combining the results of 12 studies was found to be 1.03 (95% CI: 1.01 - 1.05).

The I^2 value is the percentage value showing that the variance between studies is due to heterogeneity rather than chance. The I^2 value being 0.00% shows that there is no heterogeneity and the effects of the phytase enzyme on the examined parameters (FI and DLWG) are similar.

Table 6. Analysis of variance for subgroups for feed consumption and daily live weight gain in broiler chickens

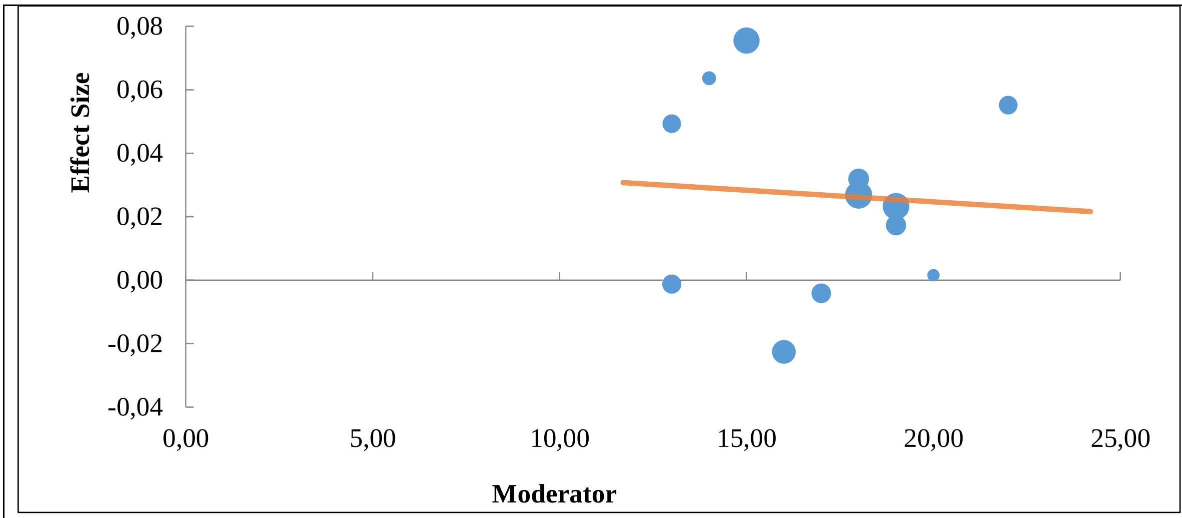
Analysis of variance	Sum of squares (Q*)	df	P values
Between / Model	0.00	1	0.955
Within / Residual	0.15	10	1.000
Total	0.15	11	1.000
Pseudo R^2	%2.19		

Even when the publications are divided into two groups, the similarity between the results is clearly demonstrated by the analysis of variance in Table 6 and the subgroup analysis in Table 7.

When the 12 studies considered are divided into two groups (AA and BB) according to the order of data entry, it can be easily understood from Tables 6 and 7 that there is no difference between the publications in terms of being affected by the phytase enzyme.

Table 7. Subgroup analysis for feed intake and daily live weight gain in broiler chickens

No	Subgroups	Odds ratio	CI LL	CI UL	Weight %	Q	P_Q	I^2 %	T^2	T
1	Zeller et al. (2015)	1.08	0.71	1.63	18.29					
2	Akter et al. (2016)	0.98	0.62	1.55	14.95					
3	Amerah et al. (2014)	1.05	0.59	1.88	9.23					
4	Han et al. (2009)	1.03	0.69	1.53	19.64					
5	Saçaklı et al. (2015)	1.02	0.68	1.54	18.90					
6	Lim et al. (2001)	1.00	0.57	1.76	9.73					
7	Swiatkiewicz et al. (2001)	1.06	0.59	1.89	9.26					
8	**AA**	**1.03**	**1.00**	**1.06**	**40.50**	**0.12**	**1.00**	**0.00**	**0.00**	**0.0**
9	Khan et al. (2019)	1.00	0.41	2.43	9.68					
10	Olukosi and Adeola (2008)	1.07	0.48	2.34	12.21					
11	Dos Santos et al. (2013)	1.02	0.59	1.74	25.93					
12	Karimi (2006)	1.00	0.57	1.73	24.60					
13	Lü et al. (2009)	1.03	0.61	1.74	27.58					
14.	**BB**	**1.02**	**0.99**	**1.05**	**59.50**	**0.02**	**1.000**	**0.00**	**0.00**	**0.0**
15.	**Combined Effect Size**	**1.02**	**1.01**	**1.03**		**0.15**	**1.000**	**0.00**	**0.00**	**0.0**



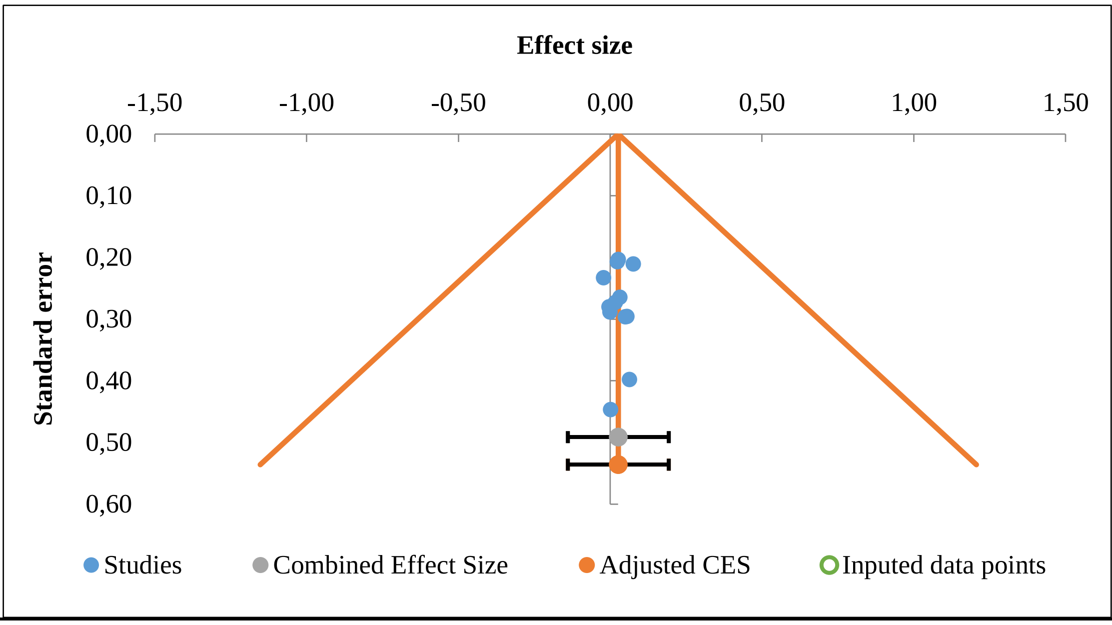
	B	SE	CI LL	CI UL	β	Z-value	P-value
Intercept	-0.35	1.92	-4.58	3.88		-0.18	0.857
Moderator	0.02	0.11	-0.23	0.26	0.58	0.14	0.889

Analysis of variance	**Q**	**DF**	**P**	**Mean square**	**F-Value**	**P-value**
Model	0.00	1	0.981	0.00	0.04	0.849
Residual	0.15	10	1.000	0.01		
Total	0.15	11	1.000			
Combined effect size	0.03					
T^2	0.00					
R^2	%0.38					

Figure 6. Moderator analysis for feed intake and daily live weight gain in broiler chickens

According to Figure 6, the regression between FI and DLWG (0.38%) was not found to be significant (P = 0.849). However, moderator analysis revealed that both parameters were similarly affected by the phytase enzyme (P = 0.981).

Funnel Plot



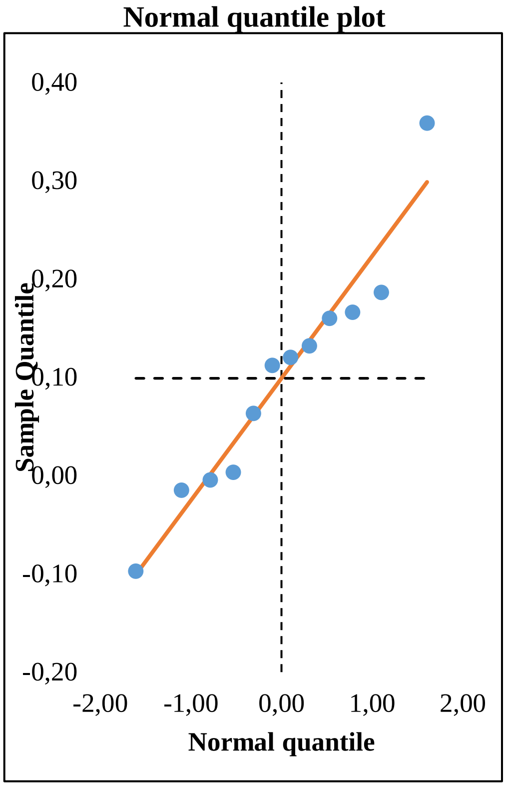
Combined effect size	Observed	Heterogeneity	
Log Odds Ratio	0.03	Q	0.15
SE Log Odds Ratio	0.08	P_Q	1.000
CI LL	-0.14	I^2	0.00 %
CI LL	0.19	T^2	0.00
PI LL	-0.14	T	0.00
PI LL	0.19		

Combined effect size	Adjusted	Trim and Fill	On
Log Odds Ratio	0.03	Estimator for missing studies	Leftmost Run/Rightmost Run
SE Log Odds Ratio	0.08	Search from mean	Left
CI LL	-0.14	Number of missing studies	0
CI LL	0.19		
PI LL	-0.14		
PI LL	0.19		

Figure 7. Trend analysis for feed intake and daily live weight gain in broiler chickens

The fact that there is no bias among the selected publications is demonstrated by the effect width distribution on the Y axis of the funnel plot in Figure 7, as well as the values of $I^2 = 0.00\%$, $T^2 = 0.00$ and $P_Q = 1.000$ of the Cochran Q statistic given for heterogeneity at the bottom of the figure. This can be interpreted as the heterogeneity between studies being not significant. As a matter of fact, the significant intersection of point estimates and confidence intervals of the studies given in the graph visually supports this finding. In the figure, the accumulation around the Y axis results in the standard error being less than 0.50 in the studies, so the effect of the phytase enzyme is similar to the low standard error in the studies.

According to the Failsafe N test, the overall Z value is 0.34, the Failsafe–N value is 0, the dc value is 0 and the Chi-square (0.697) is insignificant, proving that the effect of the phytase enzyme on both parameters is the same. Failsafe-N analysis (0) shows that among the 12 studies entered into the meta-analysis program, no study was found that increased the P value, that is, opposed to the effect of the phytase enzyme (Figure 8).



Failsafe N tests	
Rosenthal	
Overall Z-score	0.34
Failsafe-N	0
Ad-hoc rule	Doğru
Gleser and Olkin	
Number of unpublished studies	11
Orwin	
Combined effect size	0.03
Criterion value d_C	0
Mean fail safe studies d_{FS}	-0.69
Failsafe-N	1
Fisher	
Failsafe-N	20
$p_{(Chi\text{-}square\ test)}$	0.697

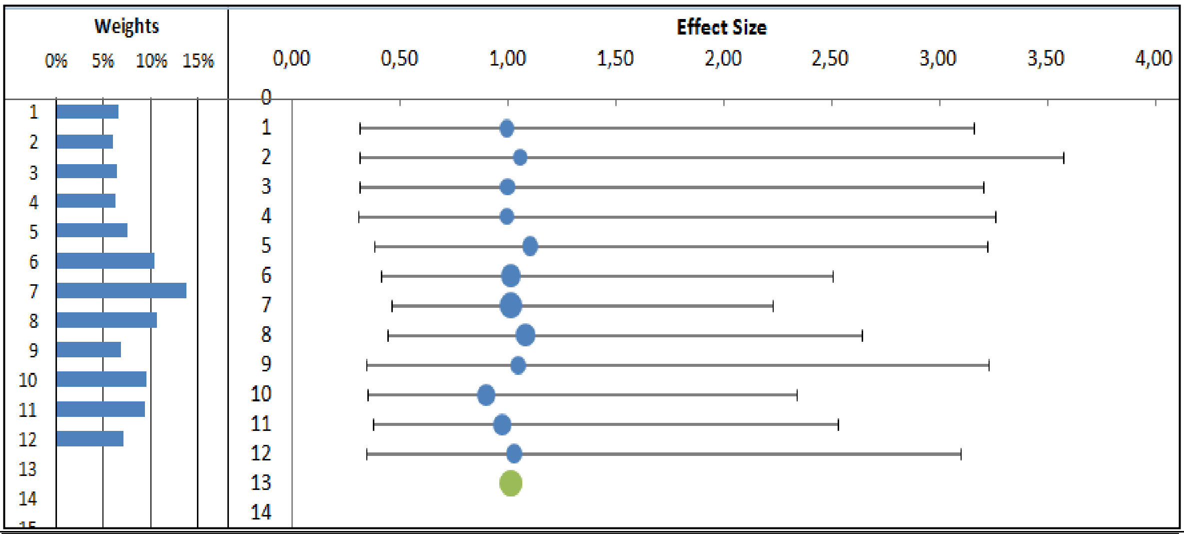
Figure 8. Failsafe N analysis for feed consumption and daily live weight gain in broiler chickens

3.3. Bone Ca and P Content

The result of the data analysis (Forest plot) made by taking into account the control and effective phytase dose of 12 publications studied in different centers between 2001 and 2018, where bone Ca and P content were considered together as parameters, is given in detail in Figure 9 below.

Figure 9 shows the meta-analysis diagram (Forest plot) in which the effect widths of the studies included in the meta-analysis are given. According to this diagram, it is seen that the effect width of the 12 studies is on the same values when looking at the Odds Ratio values stated both in point and numerical terms, and all 12 studies contribute to the combined result of the meta-analysis. The study that contributed the most to the overall result was Viveros et al.(2002) with a weight ratio of 13,66 %. This study has the closest weight ratio (10.67%) to Tang et al. (2012)'s study is followed.

As seen in Figure 9, as a result of the confidence interval determined according to the length of the horizontal lines passing through the circles (●) representing the effect widths, the widest confidence interval was found by Han et al. (2009). In addition, it is seen that 12 of the 12 studies used in the research have a positive effect width. The positive effect width indicates that the effect width is in favor of the experimental group. In addition, the fact that the effect width is greater than zero shows that the effect of phytase enzyme coefficient on both parameters (bone Ca and P content) is statistically significant and positive.



Studies	Odds ratio	CI LL	CI UL	Weight %
1.Lim et al. (2001)	0.99	0.31	3.16	6.53
2.Han et al. (2009)	1.06	0.51	3.57	5.90
3.Walk et al. (2012)	0.99	0.31	3.20	6.38
4.Tizziani et al. (2016)	0.99	0.30	3.26	6.21
5.Santos et al. (2008)	1.10	0.38	3.22	7.52
6.Küçükyılmaz et al. (2017)	1.01	0.41	2.50	10.39
7.Viveros et al. (2002)	1.01	0.46	2.23	13.66
8.Tang et al. (2012)	1.08	0.44	2.64	10.67
9.Carlos et al. (2015)	1.05	0.34	3.22	6.86
10.Bingöl et al. (2009)	0.90	0.35	2.33	9.46
11.Bilal and Hilkat Aksakal (2004)	0.97	0.37	2.53	9.29
12.Ajith et al. (2018)	1.03	0.34	3.10	7.12

Figure 9. Effect size of effect for bone Ca and P content in broiler chickens

Table 8. Combined effect size and heterogeneity analysis for bone Ca and P content in broiler chickens

Combined effect size	Values
Odds Ratio	1.01
CI Lower limit	0.98
CI Upper limit	1.05
PI Lower limit	0.98
PI Upper limit	1.05
Z-value	0.79
One-tailed p-value	0.216
Two-tailed p-value	0.432
Number of incl. subjects	904
Number of incl. studies	12
Heterogeneity	
Q	0.13
p_Q	1.000
I^2	%0.00
T^2 (Odds Ratio)	0.00
T (Odds Ratio)	0.00

Table 8 shows the combined effect width and heterogeneity analysis results for bone Ca and P content in broiler chickens. As a result of the analysis, the OR value (95% CI: 1.01 0.98 - 1.05) was found by combining the results of 12 studies.

Since the Z value is less than 1 and the P value is 0.216, it is understood that the relationship between bone Ca and P content is important. The I^2 value being 0.00% shows that there is no heterogeneity and the effects of the phytase enzyme on the examined parameters (bone Ca and P content) are similar.

Even when the publications are divided into two groups, the similarity between the results is clearly evident with the analysis of variance and subgroup analysis in Tables 9 and 10.

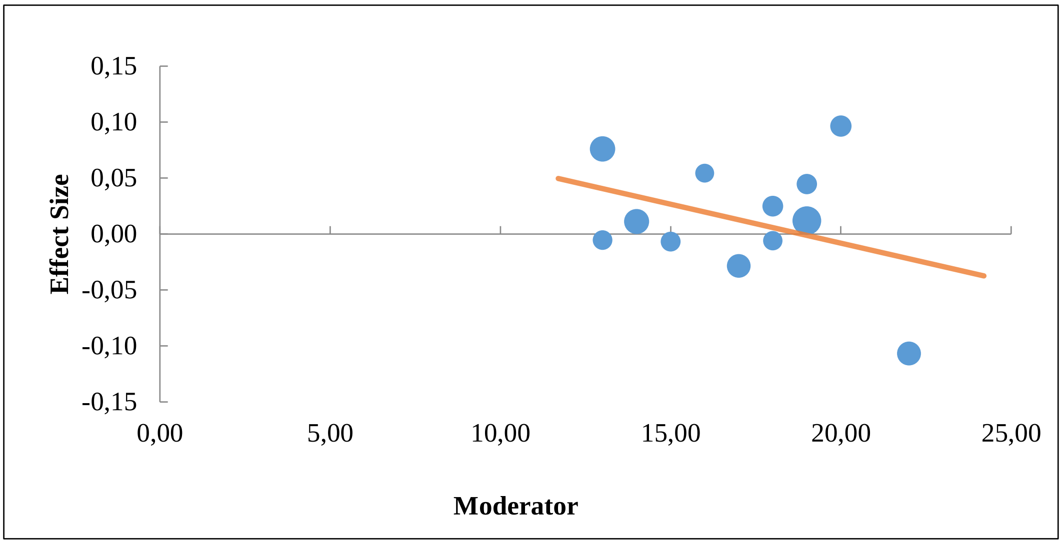
When the studies discussed are divided into two groups (AA and BB) according to the data entry order, it can be easily understood from Tables 10 and 11 that there is no difference in terms of being affected by the phytase enzyme among the 12 publications.

Table 9. Analysis of variance for subgroups for bone Ca and P content in broiler chickens

Analysis of variance	Sum of squares (Q*)	df	P values
Between / Model	0.01	1	0.939
Within / Residual	0.12	10	1.000
Total	0.13	11	1.000
Pseudo R^2	%4.67		

Table 10. Subgroup analysis for bone Ca and P content in broiler chickens

No	Subgroups	OR	CI LL	CI UL	Weight %	Q	P_Q	I^2 %	T^2	T
1.	Lim et al. (2001)	0.99	0.31	3.16	11.10					
2.	Han et al. (2009)	1.06	0.31	3.57	10.03					
3.	Walk et al. (2012)	0.99	0.31	3.20	10.84					
4.	Tizziani et al. (2016)	0.99	0.30	3.26	10.56					
5.	Viveros et al. (2002)	1.01	0.46	2.23	23.24					
6.	Tang et al. (2012)	1.08	0.44	2.64	18.14					
7.	Bingöl et al. (2009)	0.90	0.35	2.33	16.08					
8.	**AA**	**1.00**	**0.95**	**1.06**	**44.08**	**0.09**	**1.0**	**0.00**	**0.0**	**0.0**
9.	Santos et al. (2008)	1.10	0.38	3.22	18.26					
10.	Küçükyılmaz et al. (2017)	1.01	0.41	2.50	25.23					
11.	Carlos et al. (2015)	1.05	0.34	3.22	16.66					
12.	Bilal and Hilkat Aksakal (2004)	0.97	0.37	2.53	22.56					
13.	Ajith et al. (2018)	1.03	0.34	3.10	17.29					
14.	**BB**	**1.03**	**0.97**	**1.09**	**55.92**	**0.03**	**1.0**	**0.00**	**0.0**	**0.0**
15.	**Combined Effect Size**	**1.02**	**0.99**	**1.04**		**0.13**	**1.0**	**0.00**	**0.0**	**0.0**



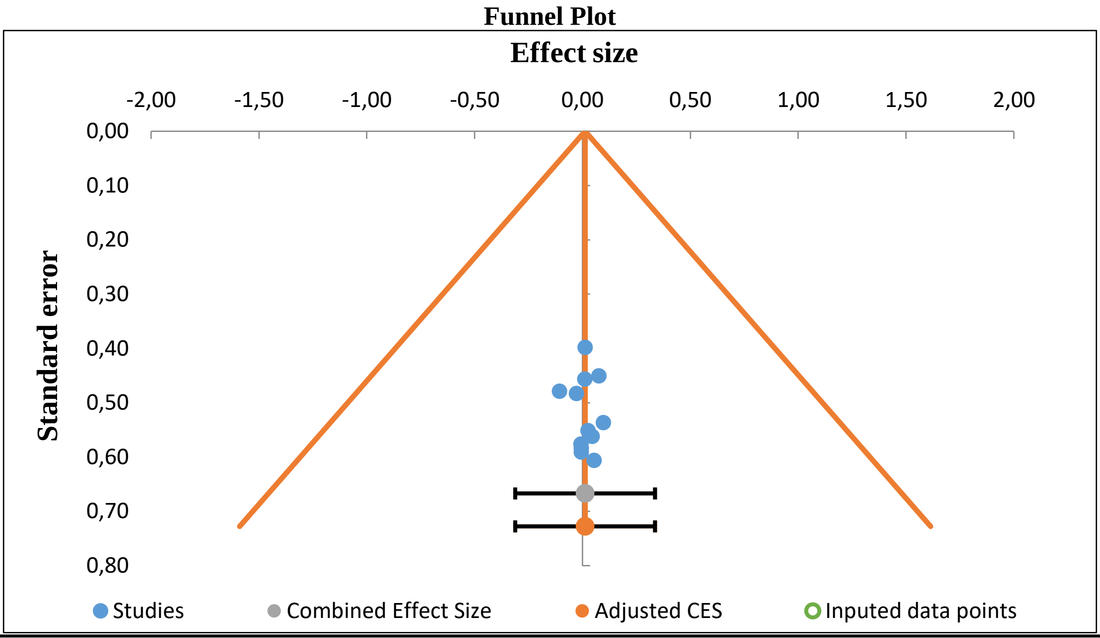
	B	SE	CI LL	CI UL	β	Z-value	P-value
Intercept	0.13	0.90	-1.85	2.12		0.15	0.884
Moderator	-0.01	0.05	-0.12	0.11	0.38	-0.13	0.894

Analysis of variance	**Sum of squares (Q)**	**df**	**p**	**Mean square**	**F-Value**	**P-value**
Model	0.02	1	0.894	0.02	1.66	0.226
Residual	0.11	10	1.000	0.01		
Total	0.13	11	1.000			
Combined effect size	0.01					
T^2	0.00					
R^2	%14.25					

Figure 10. Moderator analysis for bone Ca and P content in broiler chickens

According to Figure 10, the regression between bone Ca and P content (14.25%) was not found to be significant (P = 0.226). However, moderator analysis revealed that both parameters were similarly affected by the phytase enzyme (P = 0.894).

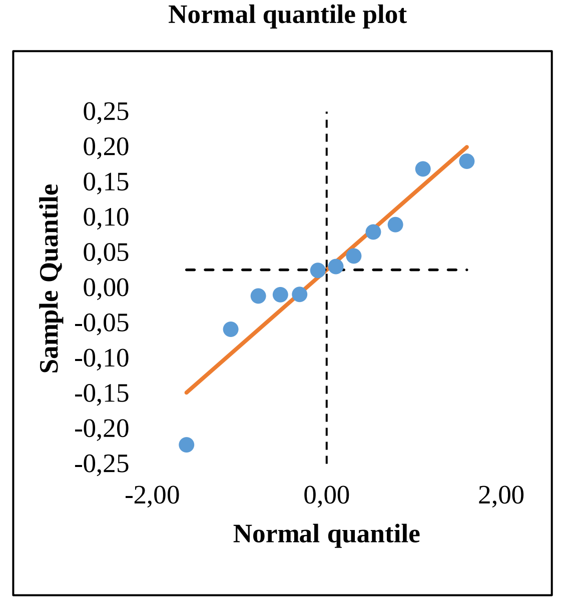
It is understood from the effect size distribution on the Y-axis of the funnel plot in Figure 11 that there is no bias among the 12 selected publications and from the values of I^2 = 0.00%, T^2 = 0.00 and PQ = 1.000 of the Cochran Q statistic given for heterogeneity at the bottom of the figure. This can be interpreted as the heterogeneity between studies being not significant. As a matter of fact, the significant intersection of point estimates and confidence intervals of the studies given in the graph visually supports this finding. In the figure, the accumulation around the Y axis results in the standard error being less than 0.70 in studies, so the effect of the phytase enzyme is similar to the low standard error in studies.



Combined effect size	**Observed**	**Heterogeneity**	
Log Odds Ratio	0.01	Q	0.13
SE Log Odds Ratio	0.15	P_Q	1.000
CI Lower limit	-0.31	I^2	0.00%
CI Upper limit	0.34	T^2	0.00
PI Lower limit	-0.31	T	0.00
PI Upper limit	0.34		

Combined effect size	**Adjusted**	**Trim and Fill**	On	
Log Odds Ratio	0.01	Estimator for missing studies	Leftmost Run	Run/Rightmost
SE Log Odds Ratio	0.15	Search from mean	Left	
CI Lower limit	-0.31	Number of missing studies	0	
CI Upper limit	0.34			
PI Lower limit	-0.31			
PI Upper limit	0.34			

Figure 11. Trend analysis for live weight and feed conversion ratio in broiler chickens



Failsafe N tests	
Rosenthal	
Overall Z-score	0.09
Failsafe-N	0
Ad-hoc rule	Doğru
Gleser and Olkin	
Number of unpublished studies	11
Orwin	
Combined effect size	0.01
Criterion value d_C	0
Mean fail safe studies d_{FS}	-0.69
Failsafe-N	1
Fisher	
Failsafe-N	19
$p_{(\text{Chi-square test})}$	0.752

Figure 12. Failsafe N analysis for bone Ca and P content in broiler chickens

According to the Failsafe N test given in Figure 12; The fact that the overall Z value is 0.09, the Failsafe-N value is 0, the dc value is 0 and the Chi-square is insignificant (P = 0.752) shows that the effect of phytase on both parameters is the same. Failsafe-N analysis (0) shows that there is no need to add an additional study to confirm the effect of the phytase enzyme.

As can be seen from Table 11, it is understood from the values of I^2 = 0.00% that there is no heterogeneity in all parameters (LW, FCR, FI, DLWG, bone Ca and P content) examined in broiler chickens. It can be seen in the calculated P (0.953, 0.955, 0.939) values that the subgroups created from the publications used are not different from each other. In terms of the parameters considered, a statistically significant (P = 0.047) R^2 value was found only in live weight and feed conversion ratio. When the studies were analyzed in terms of trend (0.06, 0.15, 0.13), it was understood that there was no heterogeneity and no significant deviation in the results. This situation is supported by the results obtained with $\chi 2$ analysis (P = 0.752, 0.697, 0.752).

Tablo 11. Summary of meta-analysis of publications investigating the effect of phytase enzyme on broiler chickens

Meta Analysis	Parameters	LW- FCR	FI-DLWG	Bone Ca-P contents
Heterogenity	I^2	%0.00	%0.00	%0.00
	Z	-3.61	3.05	0.79
Subgroup	P	0.953	0.955	0.939
Moderator	R^2	%33.88	%0.38	%14.25
	P	0.047	0.849	0.226
Trend	Q	0.06	0.15	0.13
Failsafe N	$\chi 2$	0.752	0.697	0.752

4. CONCLUSIONS

Thirty six studies were included in this meta-analysis study, which aims to determine the effect of phytase feed additive added to broiler chick rations at different doses on the parameters examined in the study.

A generally positive effect of the phytase enzyme on the parameters examined was determined. It has been revealed by meta analysis that these effects are similar to each other. In other words, it has been proven by heterogeneity and trend analyzes that these studies do not differ from each other in terms of their results.

In conclusion; Meta-analysis revealed that the effects of phytase enzyme on live weight, live weight gain, feed consumption, feed conversion ratio, bone Ca and P content parameters are similar to each other. Therefore, since the positive effect of the phytase enzyme on zootechnical parameters has been proven by this study meta-analysis, there is a need to provide a good justification before deciding on its reuse. In addition, by examining through meta-analysis the publications in which not only phytase but also other feed additives are used adequately in animal nutrition, resource waste and duplication in research can be prevented.

Conflict of Interest Declaration

This article is a research article produced from Tuğba Özdemir's Master's Thesis. There is no conflict of interest.

Researchers' Contribution Rate Declaration Summary

The research was produced with 20% contribution from Ahmet Şahin Consultancy and 80% contribution from the Graduate Student.

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