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*Research Article*

# Meta-Analysis of the Causality of Deformations in Marine Fish Larvae Culture

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The development of deformities in farmed fish is largely the result of abiotic, biotic, and xenobiotic factors, information deficiencies in optimizing nutrition, and the genetic background to which the fish are exposed in their early life stages. In general, skeletal anomalies are considered to have significant adverse effects on animal welfare, biological performance of farmed fish, product quality, and production costs. In the data obtained by the meta-analysis method, the presence of negative effects on the formal structures of fish was found, regardless of the region, duration, stage, factor, stock density, and method used to detect deformation. In this regard, in the studies considered within the deformation region/type, 46% of deformities were found in the spine, 37% in the head, and 16% in the total skeleton. In turn, the results of the meta-analysis showed that the percentages of the apparent value were 35.82% in the spine, 33.12% in the skeleton, and 31.06% in the head. The deformation rate had an overall negative effect on the functional characteristics of the fish, regardless of the variables considered. In addition, all statistically significant individual response variables had a negative effect size. In the future, advanced statistical tools such as Bayesian meta-analysis, network meta-analysis, and meta-regression analysis can be used to explore more complex data structures. The rapid development of artificial intelligence techniques will increase the efficiency of data collection and the robustness of results for meta-analysis studies in aquaculture and other fields.

## 1. Introduction

Marine fish farming is now an industry that has become an important source of economic profit, employment, and livelihood in many countries. Due to the high economic value of the species produced and their suitability for intensive production, their market share is growing daily. In this context, marine fish farming accounts for 7.3 million tons of the 30.8 million tons of seafood produced worldwide [1]. With this intensive production, problems related to production have also arisen. The goal of good production is to maintain the characteristics of the morphologically natural forms of farmed fish in terms of quality and quantity. However, even with the best breeding techniques, some morphological disorders can occur in the farmed species. Permanent differences in shape (deformities), which are readily apparent to the consumer, usually occur in the early embryological and postlarval stages of production [2]. Production defects that occur at certain times in breeding facilities also cause undesirable deformations. Theoretically, developmental defects cause phenotypic differences in individuals who genetically exhibit the same traits under the same environmental conditions. As the increase in phenotypic changes negatively affects the feeding and swimming activities of the fish, the stress factor also comes into play [3]. However, it is not yet clear whether individuals with deformities in their embryonic and postembryonic stages exhibit the same characteristics throughout their lives. Although the causes of vertebral deformities in juvenile and adult fish are considered to be notochord deformities that occur during the larval period, the study of fish ontogeny development is understood to cause skeletal deformities in alternate biological processes. The development of deformities in reared fish is largely the result of abiotic, biotic, and xenobiotic influences, information deficits in diet optimization, and the genetic background to which fish are exposed in their early life stages [4]. Abiotic factors, such as photoperiod, light intensity, dissolved oxygen, and carbon dioxide, and high water current [5–11], such as nutritional (nutritional imbalance) deficiencies (lysine, tryptophan, phenylalanine, vitamin A (VA), C, D, E, K, *n*-3 highly unsaturated fatty acid, phospholipid, phosphorus, manganese, and zinc) swimbladder problems, stock densities, manipulations, parasites, bacterial, and viral infections, have an intense effect on deformations [6, 12–19].

The protruding abdominal areas, relatively small head structure, and scale deformities observed in fish in the first years of production took on other shapes as the production level increased and the number of deformed individuals increased. In addition, some chemicals are known to cause deformations in fish larvae [20–24]. Contaminants mixed with water such as dioxins, polychlorinated biphenyls, and tributyltin can negatively affect the mineralization process and cause the weakening of the skeletal structure [25–29]. Inevitably, the genetic background [30–34] can be shown as the main causes of these deformations. The protruding abdominal regions, relatively small head structure, and scale deformities previously observed in fish took other forms as production levels increased and the number of deformed individuals increased. In addition, inappropriate net structures caused the formation of irregular scratches on the scales and skin of the fish, which became apparent as excessive mucus production and desquamation during the marketing phase [7, 35, 36]. In addition, problems with poor coloration (the color of the fish deviates from its natural color) have increased. Subsequently, the increase in production capacity and survivability over the years has led to various deformation structures and related production problems. In this context, skeletal deformities are defined as one of the most important biological problems in contemporary production. Skeletal deformities are generally observed in the axial skeleton, the jaw and operculum, the fin carrier, and the complex structures of the tail bone [7, 17, 37–39]. The most common types of skeletal deformations of the axial skeletal structure under aquaculture conditions are lordosis, kyphosis, and scoliosis [15, 17, 40–42]. These deformation types are intensively studied in red sea bream (*Pagrus major*), gilthead sea bream (*Sparus aurata*), European sea bass (*Dicentrarchus labrax*), Japanese flounder (*Paralichthys olivaceus*), Atlantic salmon (*Salmo salar*), rainbow trout (*Oncohrynchus mykiss*), Senegal sole (*Solea senegalensis*), Atlantic cod (*Gudas morhua*), Yellowtail (*Seriola sp.*), and grouper (*Epinephelus sp.*) farmed in different regions of the world [37, 42–49]. Sometimes very different types of deformation can be detected at the same time in the same individual. These types of deformation can be detected by staining the bone cartilage, observation under the microscope, X-rays, and by the naked eye. Skeletal development is important for external morphology and functional mobility during juvenile rearing, and skeletal deformities increase production costs [50, 51]. Movement difficulties, poor growth, high mortality, and diseases in deformed fish cause great economic losses [36, 51–54]. It has been noted that it is difficult to obtain official data on the incidence of deformities from commercial hatcheries, but generally, 7%–20% of deformed individuals occur, and this rate may even increase to 45%–100% from time to time [37, 39, 43–45, 47, 55–60]. In the first stages of production, fish are stunned in high salinity to separate individuals without a swim bladder. Additionally, deformed fish are separated on illuminated tables before being sent to net cages and/or earthen ponds. However, despite all these practices, deformed individuals are encountered in the later stages of production. Since deformed fish are not preferred by consumers, market opportunities, and prices for these products are lower. In addition, these individuals must be separated from other individuals at the hatchery, which increases production costs. It is estimated that European aquaculture suffers annual losses of 50 million euros due to deformities [51]. This situation also puts a lot of pressure on the sustainable development of the aquaculture industry [51, 53, 54, 61, 62]. For this reason, researchers tend to find the reason for these negative characteristics that occur in production with the new techniques that they constantly use.

In a meta-analysis, the results of multiple studies on specific topics are collected independently, combined, and analyzed using statistical methods. Thanks to this method, it can also be defined as a measure that expresses the extent and direction of the relationship between variables. A meta-analysis is a useful approach for extracting and integrating information from different studies. It recognizes the need to integrate and synthesize experimental observations using a quantitative approach [63–66]. For this purpose, a meta-analysis was conducted, which is a systematic literature review, and used. The goal of the study conducted in this context is to analyze the results of research on deformities in marine fishes using the method of meta-analysis, to evaluate the cause–effect relationships of the problems uncovered so far, and to develop different approaches for new research.

## 2. Materials and Methods

In the study, the data on the deformation rate of control and experimental groups in all scientific articles on marine fish larvae farming were searched. Thus, it was investigated whether the deformation rate affects the deformation region/type and the factors that cause the deformation. For this purpose, a meta-analysis was conducted, which is a systematic literature review, and used. In the data analysis, the appropriate methods for the data type were selected from the possible combinations of research results. In this study, subgroup analysis for deformity region/type and causes was performed following the guidelines of empirically based published studies for researchers [67]. First, the characteristics of these studies were coded. Then, effect sizes were calculated using a common scale. Finally, the moderation effects of the studies on the outcome measure were examined.

In addition to the effect of the deformation rate on the deformation area in the hypotheses established for the study, the continent where the study was conducted was evaluated in terms of working time, fish production stage, deformation factor, stocking density, and method of determining deformation. A literature review was then planned to determine the validity of these hypotheses [68, 69]. To define the problem under study, the fish species studied, deformation factor, working time (day), fish production stage, number of fish used for analysis ($n$), stocking density (individual/l), deformation analysis method, statistical analysis method, significance value ($P$), deformation type, and deformation rate (%; control and experimental) were analyzed by meta-analysis method.

In the data collection, a literature search strategy was first established for the studies to be included in the meta-analysis of the factors affecting the development of deformations. For this purpose, the Web of Science (WOS), Google Scholar, and Scopus databases were searched, covering the years 1997–2022 (June). The search term was ((“deformities” AND “marine fish larvae”), (“abnormalities” AND “marine fish larvae”), (“malformation” AND “marine fish larvae”), (“osteological abnormalities” AND “marine fish larvae”), and (“skeletal deformation” AND “marine fish larvae”)).

As a result of the search, 1,700 references were obtained. The search strategy was changed due to a large number of literatures, the fact that reviewing individual abstracts can lead to errors, and the number of literatures that did not meet the acceptance criteria, we had previously established in the Google Scholar database. It was decided to use the WOS database because it was believed that randomized controlled trials, one of the acceptance criteria, could be obtained at a higher rate than in the Google Scholar database. In addition, in order to reduce the number of literatures to some extent and to examine the lower number of relevant literatures in more detail, the terms “deformities,” “marine fish larvae,” and “aquaculture” were set as keywords.

In accepting the literature on the topic, English-language full-text articles were first identified. In addition, articles that were evaluated first asked about early developmental stages (larval stage, weaning, pregrowth, and juvenile fish), cause of deformity (feeding, production model, and other factors), type of deformity (head, spine, and skeleton), and rate of deformity. Articles that did not meet the above criteria and those that did not provide statistical results were not included in the study.

In the coding phase of the studies, after the literature was transferred to the Mendeley program, the title and abstract were first reviewed and evaluated. After the preliminary evaluation, the full text of all the literature to be analyzed was obtained. The literature to be included in the analysis was coded by full-text evaluations according to the inclusion and exclusion criteria. The number of literatures to be included in the search and review is shown in the PRISMA flowchart [69]. The PRISMA flowchart for the literatures was included in the analysis, inspired by the work of Cozer et al. [70] (Figure 1).

In coding the studies, the studies included in the analysis were grouped under the heading of diet, production system, and other factors to show the general cause of deformation. These studies are listed in Table 1.

*2.1. Data Analysis.* In the effect size meta-analysis, it was necessary to calculate the measures of the outcome variables (effect sizes) for each of the studies before numerically combining each research article included in the study. In calculating the effect size, the values of “OR” were used as the basis for evaluating the overall effect size in the analyzes conducted for binary data. The limit of statistical significance in the evaluation of the overall effect meant that the risk of an $OR > 1$ outcome was increased [101–103]. The minus (−) sign at the beginning of the effect values represents the control group; the plus (+) sign indicates that the effect was positive for the experimental group. When the effect size was zero or close to zero, it indicated that there was no result for or against the control and experimental groups. A composite effect size of 0.80 and above was considered a significant effect; values between 0.50 and 0.79 were considered moderate, and values below 0.50 were considered no effect [104]. If the study had a homogeneous distribution, the fixed effects model was used; if the distribution was not homogeneous, the random effects model was used [105].

To adjust or calibrate the results of studies meeting the criteria to a common scale, effect sizes were calculated using odds ratios and Hedge’s $g$ values. Statistical analyses were performed using the metaessentials workbook Version 1.4, which is licensed under Creative Commons. Data were interpreted using the user’s guide under the Attribution-Non-Commercial-ShareAlike 4.0 International License [106] and developed after [107]. Subgroup and moderator analyses were performed when heterogeneity (I2) was high [108]. This allowed the researchers to further investigate the role of the different variables.

After calculating the deformation rate and effect size values of each trial in the control and experimental groups, the I2 statistic was reviewed for heterogeneity analysis. I2 is the heterogeneity ratio of the total change in the observed effect. Heterogeneity is related to the percentage of variance disclosure of the available studies. Heterogeneity increases as the percentage of disclosure increases [66]. When assessing heterogeneity, a heterogeneity rate (I2) of less than 25% is considered absent, 25%–50% is considered low, 51%–75% is considered moderate, and more than 75% is considered high [103]. This test tests the null hypothesis that all items rate the same effect. This analysis is used to determine if there is a statistically significant variance [109].

Publication bias above a certain level affects the average effect size to be calculated and makes it higher than it should be [110]. For this reason, publication bias is determined by calculating Kendall’s tau coefficient from the “funnel plot” graph, and another statistic of Begg and Mazumdar’s rank correlations. If there is no publication bias, this coefficient should be close to 1 and the double-tailed $p$-value should not make a significant difference, i.e., the $p$-value will be greater than 0.05 [103]. In addition, the results were interpreted using Orwin’s number and Egger’s regression analysis to

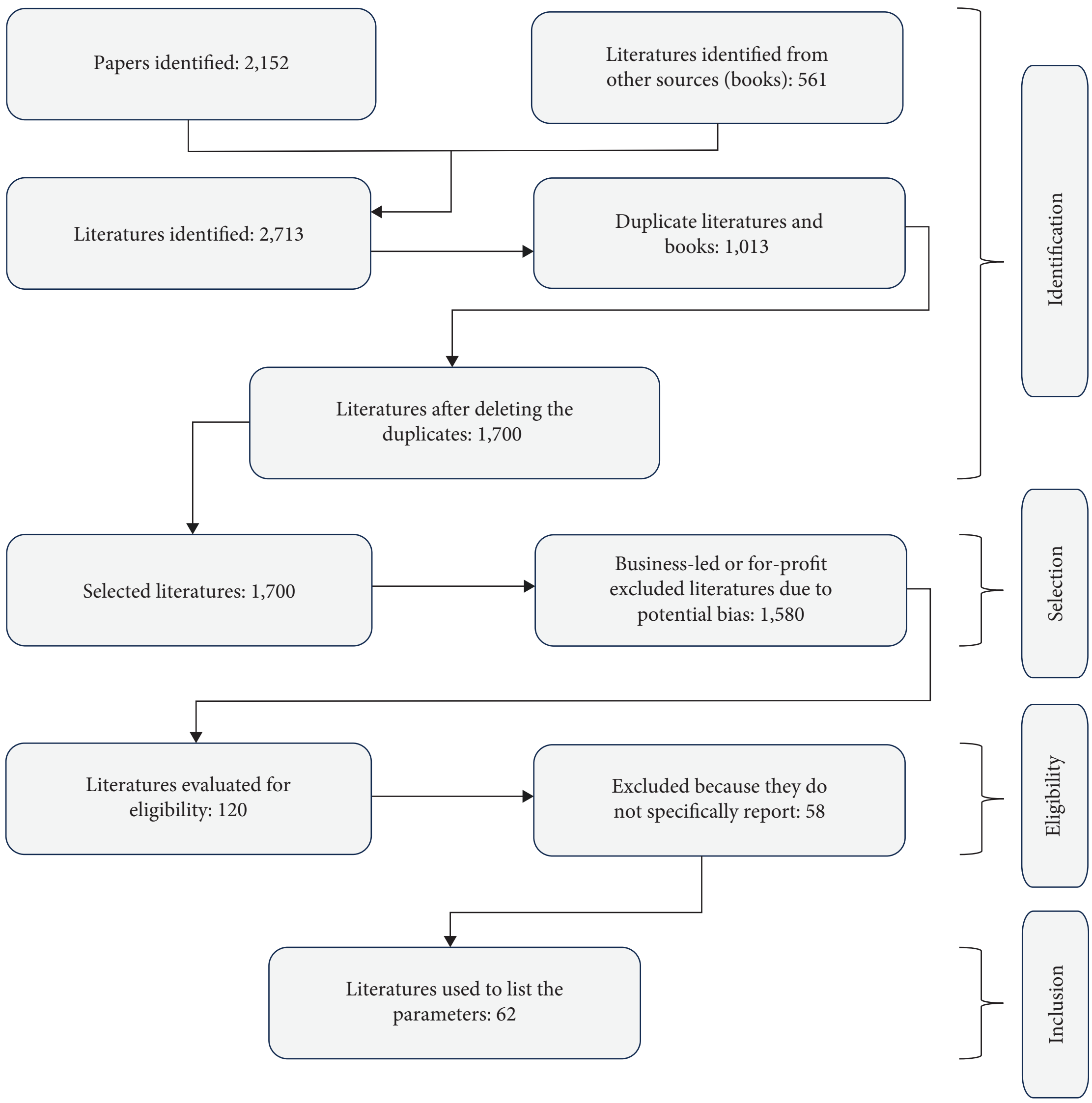



Figure 1: Flowchart showing the four stages of the systematic review (PRISMA) conducted to identify the literatures underlying deformations in marine fish larval culture.

reset the statistically significant effect of the deformation rate in the meta-analysis.

A meta-analysis was performed between the deformation rates using the studies that compared the percent change between the deformation region/type and cause between the control and experimental groups, which are included in Table 1. The I2 statistic was used for heterogeneity analysis. When this value was above 50% and the $p$-value of the heterogeneity test ($Q$) was significant ($p \leq 0.05$), the analysis was performed with the random effects model. These variables were working time, stock density, deformation detection analysis methods, deformation region/type (head, spine, and skeleton), deformation factors (feeding, production model, and other factors), and stage (larval stage, weaning, on growing, and juvenile). Publication bias was visualized with a funnel plot and quantitatively defined with the Begg–Mazumdar test, which is preferable to Egger regression because it considers smaller samples [111, 112]. All tests were performed at a 95% confidence level (CI), and all $p$-values less than 0.05 were considered significant.

## 3. Results

The following are the outcome issues:

(1) Location of deformation zone/type (head, spine, and skeleton).

(2) Deformation factors (feeding, production model, and other factors).

(3) It consists of the publications considered for the deformation stage (larval stage, weaning, on growing, and juvenile).

In the studies examined, it was found that the continent, working time, phase, factor, stocking density, and variables considered by the deformation detection method of the

Table 1: Results of the studies on the deformation rate of the fish to find the cause of deformation.

| Authors | Year | Country | Species | Factor | Duration (day) | Stage | Density (individual/l) | Deformation analysis method | Deformation region | Deformation | Def. (cont.) (%) | Def. (exp.) (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Giebichenstein et al. [71] | 2022 | Germany | *Dicentrarchus labrax* | Nutrition | 50 | Early weaning | 50 | Staining | Skeletal | Vertebral compression | 1 | 27.3 |
| | | | | | | | | | Arch | Deformed | 4 | 25.675 |
| | | | | | | | | | Skeletal | Lordosis | 8 | 26.82 |
| | | | | | | | | | Skeletal | Kyphosis | 0 | 28.72 |
| Fu et al. [72] | 2021 | Taiwan | *Trachinotus ovatus* | Nutrition | 8 | Larvae | 40 | Microscope | Jaw | Total deformed | 23 | 31 |
| Olsvik et al. [73] | 2021 | Norway | *Melanogrammus aeglefinus* | Abiotic (oil) | 243 | Growth | 5975 ± 260 (per tank) | Staining, X-ray | Skeletal | Vertebral compression | 3 | 11.6 |
| | | | | | | | | | Arch | Total deformed | 17 | 51.6 |
| Sivaramakrishnan et al. [74] | 2021 | India | *Chanos chanos* | Nutrition | 18–63 | Weaning | 100 | Microscope | Skeletal | Opercula malformation, scoliosis, lordosis, coiled vertebral column | 11.5 | 7.75 |
| Martins et al. [75] | 2019 | Portugal | *Argyrosomus regius* | Nutrition | 50 | Weaning | 44 | X-ray | Skeletal | Vertebral compression, vertebral fusion, deformed arch, lordosis | 30 | 39 |
| Hansen et al. [76] | 2018 | Norway | *Gadus morhua* | Nutrition | 45–170 | Larvae, juvenile | 80 | Staining, microscope | Jaw | Total deformed | 17.16 | 17.66 |
| Iwasaki et al. [77] | 2018 | Japan | *Epinephelus bruneus* | Biotic (swimbladder) | 200 | Larvae, Juvenile | | Staining, X-ray | Skeletal | Lordosis, kyphosis, saddleback-like syndrome, vertebrae fusion, deformed vertebrae | 0 | 2.5 |
| | | | | | | | | | | | 0 | 20.85 |
| | | | | | | | | | | | 0 | 20.4 |
| Zhou et al. [78] | 2018 | China | *Seriola lalandi dorsalis* | Nutrition | 12 | Larvae | 30 | Staining | Jaw | Total deformed | 17 | 11.5 |
| Partridge and Woolley [79] | 2017 | Australia | *Seriola lalandi* | Nutrition | 23 | Larvae | 60 | Cobcroft | Jaw | Total deformed | 16.5 | 16.6 |
| Katan et al. [80] | 2016 | Canada | *Gadus morhua* | Nutrition | 192 | Juvenile | 500 | Staining | Skeletal | Lordosis, scoliosis, stargazer, and deformed lower jaw | 0 | 7.6 |
| | | | | | 558 | Market size | | Eye | Skeletal | | 0 | 25.4 |
| | | | | | 192 | Juvenile | 50 | Staining | Skeletal | | 0 | 9.9 |
| | | | | | 558 | Market size | 0.46 | Eye | Skeletal | | 0 | 40.26 |
| Puvanendran et al. [81] | 2015 | Norway | *Gadus morhua* | Abiotic (temperature) | 1 | Larvae | | Photograph | Spinal | Total deformed | 2.4 | 3.4 |
| | | | | | | | | Eye | Spinal | Total deformed | 2.6 | 3.55 |
| Boglino et al. [82] | 2012 | Spain | *Senegalese sole* | Nutrition | 50 | Larvae | 110 | Staining | Head | Cranial deformities, head height, interorbital distance, pseudoalbino | 1.9 | 95.1 |
| Johannsdottir et al. [83] | 2014 | Island | *Gadus morhua* | Nutrition | 42 | Larvae | 60 | Staining | Skeletal (jaw, operculum, snout, swimbladder) | Lordosis, gaping | 16.7 | 1.7 |
| | | | | | 160 | Larvae | 67 | Staining | Skeletal (jaw, operculum, snout, swimbladder) | | 1.8 | 0 |

Table 1: Continued.

| Authors | Year | Country | Species | Factor | Duration (day) | Stage | Density (individual/l) | Deformation analysis method | Deformation region | Deformation | Def. (cont.) (%) | Def. (exp.) (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Richard et al. [84] | 2014 | Portugal | *Senegalese sole* | Nutrition | 39 | Larvae | 95 | Staining | Skeletal (spinal and fins) | Vertebral fusion and atrophy, malformed/fused neural and hemal arch and/or spine, malformed/fused soft ray, malformed pterygiophore (deformed, absent, fused, supernumerary), malformed parhypural/hypural (deformed, absent, fused, supernumerary), malformed epural (deformed, absent, fused, supernumerary), malformed parapophysis, malformed opercula | 97 | 84 |
| Skalli et al. [85] | 2014 | Spain | *Dicentrarchus labrax* | Nutrition | 40 | Larvae | 60 | Staining | Skeletal (head, trunk, tail) | Total deformed | | 50 |
| Negm et al. [86] | 2013 | Australia | *Latris lineata* | Nutrition | 43 | Larvae | 10 | Staining | Skeletal (spine) | Compressed vertebra, scoliosis, kyphosis | 31 | 39.14 |
| | | | | | 43 | | | Staining | Jaw | Curled and abraded, abnormal | 5 | 81.4 |
| | | | | | 25 | | | Staining | Jaw | Short, thickened, or twisted | 46 | 54 |
| Prestinicola et al. [87] | 2013 | Greece | *Sparus aurata* | System | 105 | Juvenile | 100 | Staining | Fin | Heterotopic, mineralized skeletal element in the caudal fin, partially fused epurals; partially fused the second and third hypurals, heterotopic mineralized element in the caudal region | 50.74 | 94.46 |
| Boglino et al. [82] | 2012 | Spain | *Senegalese sole* | Nutrition | 38 | Larvae | 80 | Staining | Skeletal (cranium, vertebral column, and caudal fin complex) | Fusion, compression, deformed vertebral centrums, torsion, and scoliosis | 74.2 | 76.56 |
| Hansen et al. [88] | 2011 | Norway | *Gadus morhua* | Nutrition | 75 | Larvae | 28 | Microscope | Skeletal | Scoliosis | 25 | 12 |
| Zouiten et al. [89] | 2011 | Tunis | *Dicentrarchus labrax* | System (mesocosm) | 37 | Larvae | 3 | Eye, staining | Skeletal | Lordosis, scoliosis, or kyphosis | | 26 |
| | | | | System (intensive) | | | 90 | Staining, eye | Skeletal | | 0 | 43 |
| Penglase et al. [90] | 2010 | Norway | *Gadus morhua* | Nutrition | 120 | Juvenile | 100 | X-ray | Skeletal (vertebra, jaw) | Lordosis | 75.3 | 76 |
| Cobcroft and Battaglene [91] | 2009 | Australia | *Latris lineata* | Abiotic (tank color) | 44 | Larvae | 7.5 | Microscope | Jaw | Slightly short lower, slightly snub nose | 21 | 48.8 |
| Engrola et al. [92] | 2009 | Portugal | *Senegalese sole* | Nutrition | 20 | Weaning | 104 | Staining | Skeletal (head, fin) | Deformed, absent, fused, supernumerary | 33.6 | 28.9 |

Table 1: Continued.

| Authors | Year | Country | Species | Factor | Duration (day) | Stage | Density (individual/l) | Deformation analysis method | Deformation region | Deformation | Def. (cont.) (%) | Def. (exp.) (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Faulk and Holt [93] | 2009 | USA | *Paralichthys lethostigma* | Nutrition | 35 | Larvae | 15 | Photograph | Skeletal | Lordosis | 0 | 17.03 |
| Fernández et al. [17] | 2009 | Spain | *Senegalese sole* | Nutrition | 41 | Larvae | 50 | Staining | Skeletal (cranium, vertebral column, caudal fin) | Total deformed | 83.75 | 98.2 |
| Nhu et al. [94] | 2009 | Belgium | *Rachycentron canadum* | Nutrition | 18 | Larvae | 50 | Microscope | Skeletal | Total deformed | 4.4 | 4.45 |
| Saavedra et al. [95] | 2009 | Portugal | *Diplodus sargos* | Nutrition | 25 | Larvae-weaning | 80 | Staining | Skeletal (dorsal vertebra) | Lordosis | 40 | 25 |
| | | | | | | Larvae | | | Skeletal | Vertebral compression | 84 | 76.5 |
| Fernández et al. [96] | 2008 | Spain | *Sparus aurata* | Nutrition | 60 | Weaning | 100 | Staining | Jaw | Undeveloped premaxilla | 14 | 26 |
| | | | | | 61 | | | | Head | Deformed lower and upper jaw | 16 | 31 |
| | | | | | 60 | | | | Skeletal (vertebral column, caudal fin) | Lordosis, kyphosis | 13.33 | 46.88 |
| Nguyen et al. [16] | 2008 | Japan | *Pagrus major* | Nutrition | 30 | Larvae | 20 | Staining | Skeletal (vertebral column, neural, and hemal spines) | Jaw deformity, pugheadness, lordosis and kyphosis, fused vertebral centrum, deformity in interneural spine, deformity in preural centra | 52.7 | 40 |
| Imsland et al. [97] | 2006 | Island | *Gadus morhua* | Abiotic (temperature) | 93 | Juvenile | 100 | Staining, eye | Skeletal (vertebra, operculum, jaw) | Severe S-shaped spinal column, lack of operculum or deformed jaw | 14.2 | 4.1 |
| Opstad et al. [98] | 2006 | Norway | *Gadus morhua* | Nutrition | 50 | Larvae | 100 | Staining | Skeletal (spinal) | S-shaped spinal column | 0.3 | 5.7 |
| Cobcroft et al. [99] | 2004 | Australia | *Seriola lalandi* | System | 16 | Larva | 60 | Cobcroft | Jaw | Malformed, lowered hyoid arch | 0 | 22 |
| Koumoundouros et al. [100] | 1997 | Greece | *Sparus aurata* | System | 85–100 | Pregrowth | 36,000 (finally) | Macroscopic | Head | Abnormal left and right gill cover | 0 | 15.6 |
| | | | | | 65–85 | Weaning | | | | | 0 | 16.7 |
| | | | | | 36–64 | Larvae | | | | | 0 | 15.8 |

publication that determines the deformation were studied and the data belonging to these common factors were analyzed.

The data on the deformation rates obtained from the results of the factors considered to cause deformation in the study are shown in Table 1.

As shown in Figure 2, the effect size of each study in the meta-analysis was represented with a square symbol. The total effect size, reflecting the sum of the individual studies, was shown in black at the bottom. The width of the circles was also indicated in proportion to the weight of each paper. The result of the meta-analysis calculating the difference between the means was −0.82 (−1.48, −0.45). Thus, the relationship between the deformation rate and the control and experimental groups was significant ($p \leq 0.001$) (Table 2).

According to the hypothesis that the deformation rate has a significant relationship with the deformation location of the control and experimental groups, the I2 value was 83.95%. The $Q$-value of the heterogeneity test was 379.96 ($p \leq 0.001$), the random effects model was used, and the results were presented with the forest plot diagram in Figure 2 and the meta-analysis in Table 2.

As shown in Figure 3, the effect size of each study in the meta-analysis was represented by the round red symbol. The overall effect size reflects the sum of the individual studies, as defined by the green symbol at the bottom. The width of the circles was also indicated in proportion to the weight of the individual papers. In the meta-analysis, performed by calculating the difference between the means, 0.44 (0.17, 1.15) was found.

These results were in favor of the control group. Consequently, the relationship between the deformation rate and the control and experimental groups was significant ($p \leq 0.001$) (Table 3).

To determine the influence of the deformation rate in the publications included in the study on the deformation region/type, a $p$-value of less than 0.05 was determined. The $Q$-value (379.96) was more significant than the result of the heterogeneity test, and the statistical I2 value was calculated as 83.95. As a result of the individual studies included in the analysis, it was found that the studies examined by deformation region/type had a heterogeneous structure in the applications of the meta-analysis. Therefore, the distribution of effect sizes was evaluated as a result of the random effects model calculations. The results of the meta-analysis of 62 studies that examined the effect of region/type of deformation and were included in the study are shown in Figure 2 with the forest plot. In the analysis performed according to the random effects model, the effect size was statistically significant with a value of 0.44 (0.08–2.35; $p \leq 0.001$).

To this end, a subgroup analysis was performed to examine the effects of deformation rate on deformation region/type. The results of the subgroup analysis are shown in Figure 3 and Table 3. In the study, the deformation region/type was divided into three areas: head, spine, and skeleton. All subgroups were evaluated according to the random effects model.

When the results of the meta-analysis of the deformation zone/deformation type are examined in detail, the risk difference in the direction of the deformation zone/deformation type in an analysis of heterogeneity among them based on the head region ($Q = 154.40$, $p \leq 0.001$), the risk difference in the direction of the deformation region /type is 0.21 (0.08, 0.57) in favor of the experimental group. When analyzed among themselves based on spine region ($Q = 147.27$, $p \leq 0.001$), the risk difference toward deformation region/type is 0.36 (0.17, 0.76) in favor of the experimental group when analyzed among themselves based on skeletal structure ($Q = 59.01$, $p \leq 0.001$) based on the skeletal structure. The risk difference for per type was found to be 1.10 (0.42, 2.91) in favor of the results of the funnel scatterplot, which also serves as a visual summary of the meta-analysis data set and highlights the possibility of publication bias, are shown in Figure 4. A large proportion of the 62 studies included in this study are very close to the combined effect size and in the upper ranges. According to Figure 4, it can be said that there is no picture of publication bias. Since Kendal's tau coefficient is −0.16 and $p > 0.074$, no publication bias was observed in the studies included in the meta-analysis according to the calculated values.

Examination of the funnel plot indicates the possibility of publication bias. To confirm this finding, the Begg–Mazumdar rank correlation was used and this value was used to determine whether or not the number of studies included in the study was safe. The average effect of the included publications on study time formed a uniform and symmetrical funnel. The Begg–Mazumber rank correlation yielded a coefficient of 0.14 ($p > 0.265$) for the value of Kendal's tau (Figure 5). Therefore, the number of studies considered appeared to be valid for the overall effect size determined in the meta-analysis. In accordance with this finding, the articles of the authors who drew common conclusions in the studies on the deformation rate were used.

The average impact of the publications on the studied continent, phase, factor, stock density, and deformation method formed a uniform and symmetrical funnel. The Begg–Mazumdar rank correlation yielded a value of 0.17 ($p > 0.131$) for Kendall's tau (Figure 6). Therefore, the number of studies considered seemed to be valid for the overall effect size obtained in the meta-analysis. According to this result, the articles of the authors who had drawn common conclusions in the studies on the deformation rate were used. The results of the moderators' effect size analysis are presented in Table 4.

Regression plots and lines can be interpreted according to the steepness of the line. At run time, the regression lines with stock density were not steep, but almost straight. This meant that changing the moderator did not affect the effect size. High $p$-values supported this result for run time ($p > 0.9182$) and stock density ($p > 0.7867$). Therefore, the publications on deformation showed that the deformation rate in the different subgroups was not affected by the studied continent, phase, factor, and moderators of the deformation detection method. A steep sloping line was observed for the factor and deformation detection method, and it was interpreted that when these studies are published next year, a sharp change in effect size will be observed. However, data analysis showed that factor ($p > 0.784$) and method of deformation detection (0.7839) had no effect-on-effect size. When

| Study name | Odds ratio | CI lower limit | CI upper limit | Weight (%) |
|---|---|---|---|---|
| Giebichenstein et al. [71] | 0.027 | 0.004 | 0.205 | 0.014 |
| Giebichenstein et al. [71] | 0.121 | 0.040 | 0.363 | 0.020 |
| Giebichenstein et al. [71] | 0.237 | 0.101 | 0.556 | 0.021 |
| Giebichenstein et al. [71] | 0.012 | 0.001 | 0.207 | 0.010 |
| Fu et al. [72] | 0.665 | 0.353 | 1.253 | 0.022 |
| Olsvik et al. [73] | 0.236 | 0.064 | 0.873 | 0.018 |
| Olsvik et al. [73] | 0.192 | 0.100 | 0.371 | 0.022 |
| Sivaramakrishnan et al. [74] | 1.547 | 0.591 | 4.049 | 0.021 |
| Sivaramakrishnan et al. [74] | 1.547 | 0.591 | 4.049 | 0.021 |
| Martins et al. [75] | 0.670 | 0.371 | 1.210 | 0.023 |
| Martins et al. [75] | 0.670 | 0.371 | 1.210 | 0.023 |
| Hansen et al. [76] | 0.966 | 0.463 | 2.015 | 0.022 |
| Iwasaki et al. [77] | 0.163 | 0.008 | 3.348 | 0.009 |
| Iwasaki et al. [77] | 0.019 | 0.001 | 0.317 | 0.010 |
| Iwasaki et al. [77] | 0.019 | 0.001 | 0.326 | 0.010 |
| Zhou et al. [78] | 1.576 | 0.700 | 3.547 | 0.021 |
| Partridge and Woolley [79] | 0.993 | 0.469 | 2.103 | 0.022 |
| Katan et al. [80] | 0.057 | 0.003 | 1.024 | 0.010 |
| Katan et al. [80] | 0.057 | 0.003 | 1.024 | 0.010 |
| Katan et al. [80] | 0.014 | 0.001 | 0.245 | 0.010 |
| Katan et al. [80] | 0.014 | 0.001 | 0.245 | 0.010 |
| Katan et al. [80] | 0.043 | 0.002 | 0.764 | 0.010 |
| Katan et al. [80] | 0.043 | 0.002 | 0.764 | 0.010 |
| Katan et al. [80] | 0.007 | 0.000 | 0.124 | 0.010 |
| Katan et al. [80] | 0.007 | 0.000 | 0.124 | 0.010 |
| Puvanendran et al. [81] | 0.699 | 0.129 | 3.773 | 0.016 |
| Puvanendran et al. [81] | 0.725 | 0.141 | 3.718 | 0.016 |
| Boglino et al. [82] | 0.001 | 0.000 | 0.006 | 0.016 |
| Johannsdottir et al. [83] | 11.592 | 2.307 | 58.258 | 0.016 |
| Johannsdottir et al. [83] | 11.592 | 2.307 | 58.258 | 0.016 |
| Johannsdottir et al. [83] | 4.684 | 0.213 | 102.913 | 0.009 |
| Johannsdottir et al. [83] | 4.684 | 0.213 | 102.913 | 0.009 |
| Richard et al. [84] | 6.159 | 1.721 | 22.041 | 0.019 |
| Richard et al. [84] | 6.159 | 1.721 | 22.041 | 0.019 |
| Skalli et al. [85] | 0.005 | 0.000 | 0.084 | 0.010 |
| Boglino et al. [87] | 0.881 | 0.461 | 1.683 | 0.022 |
| Hansen et al. [88] | 2.444 | 1.145 | 5.220 | 0.022 |
| Zouiten et al. [89] | 0.007 | 0.000 | 0.111 | 0.010 |
| Penglase et al. [90] | 0.963 | 0.503 | 1.844 | 0.022 |
| Cobcroft and Battaglene [91] | 0.409 | 0.149 | 1.124 | 0.020 |
| Cobcroft and Battaglene [91] | 0.409 | 0.149 | 1.124 | 0.020 |
| Cobcroft and Battaglene [91] | 0.279 | 0.149 | 0.521 | 0.022 |
| Engrola et al. [92] | 1.245 | 0.681 | 2.275 | 0.022 |
| Faulk and Holt [93] | 0.024 | 0.001 | 0.407 | 0.010 |
| Fernández et al. [17] | 0.094 | 0.020 | 0.457 | 0.017 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.836 | 0.018 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.836 | 0.018 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.836 | 0.018 |
| Saavedra et al. [95] | 2.000 | 1.089 | 3.673 | 0.022 |
| Saavedra et al. [95] | 1.613 | 0.792 | 3.284 | 0.022 |
| Fernández et al. [96] | 0.463 | 0.224 | 0.956 | 0.022 |
| Fernández et al. [96] | 0.424 | 0.213 | 0.842 | 0.022 |
| Fernández et al. [96] | 0.174 | 0.086 | 0.352 | 0.022 |
| Nguyen et al. [16] | 1.671 | 0.951 | 2.937 | 0.023 |
| Imsland et al. [97] | 3.871 | 1.233 | 12.150 | 0.019 |
| Imsland et al. [97] | 3.871 | 1.233 | 12.150 | 0.019 |
| Opstad et al. [98] | 0.050 | 0.001 | 2.023 | 0.007 |
| Opstad et al. [98] | 0.050 | 0.001 | 2.023 | 0.007 |
| Cobcroft et al. [99] | 0.017 | 0.001 | 0.296 | 0.010 |
| Koumoundouros et al. [100] | 0.026 | 0.002 | 0.452 | 0.010 |
| Koumoundouros et al. [100] | 0.024 | 0.001 | 0.417 | 0.010 |
| Koumoundouros et al. [100] | 0.026 | 0.002 | 0.445 | 0.010 |

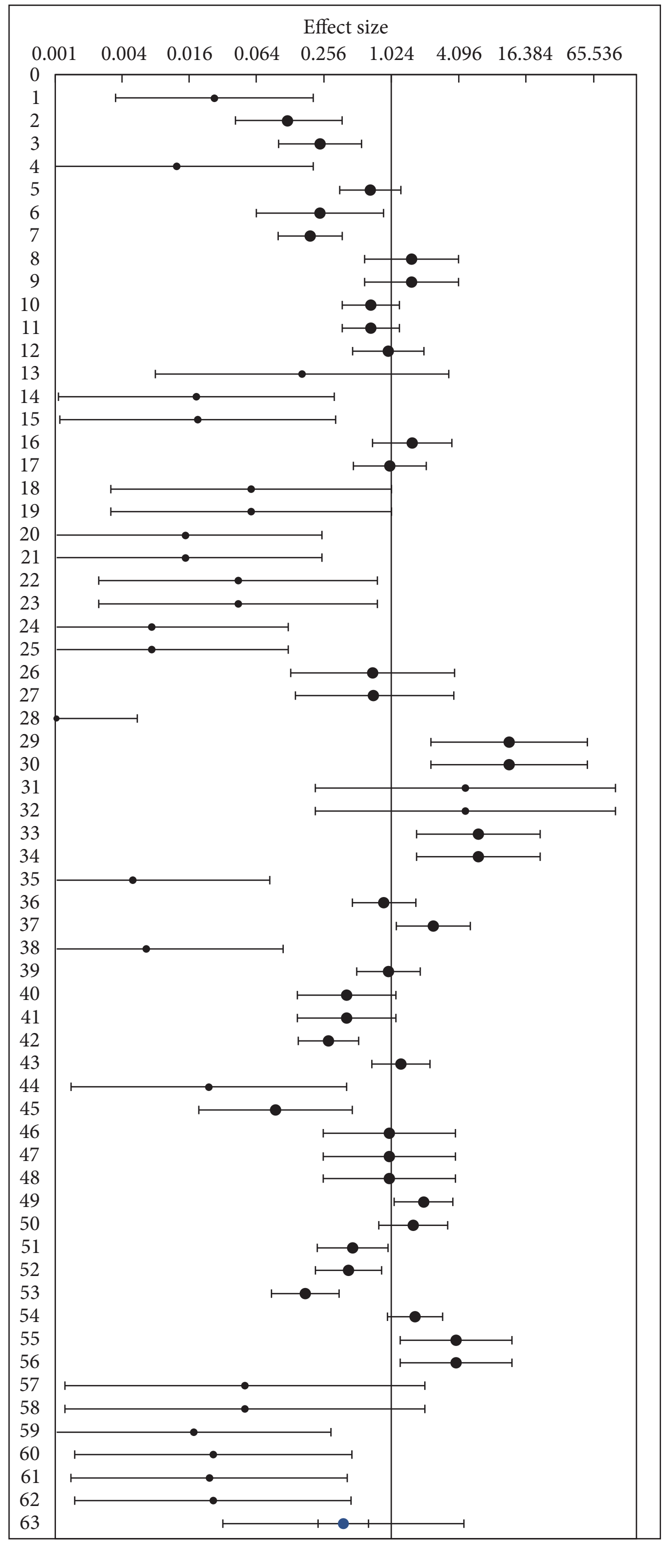



Figure 2: Forest plot diagram of deformation rate.

Table 2: Meta-analysis findings of studies using a percentage of deformation control and experimental groups.

| Overall effect size | Standard error | $Z$-value | $p$-Value | 95% Confidence interval | |
|---|---|---|---|---|---|
| | | | | Lower limit | Upper limit |
| −0.82 | 0.48 | −3.74 | 0.001 | −1.48 | −0.45 |

the phase was examined, a very steep upward line was seen, which was interpreted as a strong change in the effect size of the studies in other studies to be conducted. However, data analysis showed that the factor ($p > 0.599$) had no effect on the effect size.

## 4. Discussion and Conclusion

Shape deformities can be caused by inadequate knowledge of larval development and a lack of management and production techniques. Deformities that occur in larval production systems follow a complex structure. According to the obtained data, it was found that there were negative effects on the formal structure of fish regardless of the region, duration, stage, factor, stocking density, and method used to detect deformities. Although environmental conditions, supported by advanced application techniques, have an essential place in solving the problem, the high rate of deformation, which occurs frequently despite all developments, forces production.

Although the studies investigated were carried out on different or the same species using different or similar factors in different parts of the world, similar deformations were found in different or the same parts of the larval body [71, 85, 89]. In this analysis, we clearly understood that both abiotic, biotic, xenobiotic nutritional, and production systems have caused many different or similar deformations in many countries from Australia to Asia, Europe to Africa, and even in the Americas (Table 1).

Production of portioned fish in marine fish farming is a long and difficult process. The deformities that occur when fish reach the portion stage are observed in the first days of the larval stage, when skeletal tissue is weak or not yet differentiated, and can be seen by the naked eye in the early stages of production. The proportion of fish with abnormalities differs not only between other facilities but also between different batches in the same incubator and even among larvae from the same breeder. In addition, extreme skeletal abnormalities can occur throughout the life cycle of fish, but their development usually begins with slight abnormalities in internal elements [51]. Even when egg quality criteria are met, the negative factors that occur in the early stages of larval life can affect the larva in a short period of time. The signs of deformation can be seen at the blastomere stage of embryonic development of the egg. In this context, production techniques and environmental conditions for the management of the rootstock should be carefully monitored [113, 114]. At the beginning of the larval period, the most critical problem in the fish produced was swim bladder inflation, which caused significant problems, especially in the production of sea bream and sea bass. Although the rate of the noninflated swim bladder problem averages about 10%, this situation sometimes reaches up to 50%. The entire tank can be lost, especially due to the thickness of the oil film layer formed on the tank surface and inadequate cleaning [6, 115, 116]. Remaining larvae experience deformities of the pectoral fins, notochord/vertebral axis, and prehaemal vertebrae. Not only the noninflating of the swim bladder but also the hypertrophic (overinflated) swim bladder causes severe losses, notochord, and spinal deformities [117]. Deformities of the larval notochord that occur in the early life stages have a risk to the entire culture process.

Spinal deformities in the subsequent period are the main problem, especially in the breeding of marine fish. Different names denote disorders of the spine in different forms, and naming is done according to the type of deformity, its severity, and frequency. Lordosis is one of the most common types of deformity in farmed species, and it is commonly seen in scoliosis and kyphosis, which are other major deformities of the spine. These deformities can sometimes occur simultaneously [4]. Although it has been associated with the inflation of the swim bladder in some species, it has been associated with various causes such as feeding, water flow, and genetics in other species [6, 52, 59, 118, 119]. In addition, there are some deformities ((a) dislocation, fusion, shortening, deformation, or absence of the centers [9, 120]; (b) dislocation, compression, deformation, absence, or additional formation of the haemal and neural arches, and apophysis [16]; (c) dislocation, shortening, deformation, absence, or separation of the ribs [44, 118, 121]; and (d) platyspondyly, vertebral ankylosis, and platyspondyly [122]) that have been described. Not only the spine or related systems but also the fins are deformed. These deformities can often originate from breeding techniques, tank structure, and stocking density. The disorders, which are intensely observed under the name saddleback syndrome, are not only found in many species but also have different structures in themselves. However, it has been noted that these deformations can also be formed in the early stages of larvae, although it is not known whether they are caused by fish behavior or by nature [7]. Although these deformities affect the welfare of the animals, they do not have a decisive effect on market conditions because the main structure of the fish has not deteriorated.

Another condition that is common in fish and differs in classification is head deformities. Although they cannot be fully explained, genetic disorders, sudden temperature changes during the incubation period of eggs, parasites, environmental conditions, and the use of feeds with insufficient vitamin content, in particular, are thought to cause the development of such deformities [7, 51, 76, 96, 99]. In general, these morphological disturbances in the cephalic region adversely affect the respiratory metabolism and feed intake of the fish.

The techniques used to detect the above deformations have now reached the standard. Depending on the life stage

| Study name/Subgroup name | Odds ratio | CI lower limit | CI upper limit | Weight (%) |
|---|---|---|---|---|
| Fu et al. [72] | 0.665 | 0.353 | 1.253 | 6.084 |
| Hansen et al. [76] | 0.966 | 0.463 | 2.015 | 5.973 |
| Zhou et al. [78] | 1.576 | 0.701 | 3.547 | 5.882 |
| Partridge and Woolley [79] | 0.993 | 0.469 | 2.103 | 5.955 |
| Katan et al. [80] | 0.057 | 0.003 | 1.024 | 2.950 |
| Katan et al. [80] | 0.014 | 0.001 | 0.245 | 3.013 |
| Katan et al. [80] | 0.043 | 0.002 | 0.764 | 2.971 |
| Katan et al. [80] | 0.007 | 0.000 | 0.124 | 3.021 |
| Boglino et al. [82] | 0.001 | 0.000 | 0.006 | 4.550 |
| Johannsdottir et al. [83] | 11.592 | 2.307 | 58.255 | 4.698 |
| Johannsdottir et al. [83] | 4.684 | 0.213 | 102.904 | 2.736 |
| Skalli et al. [85] | 0.005 | 0.000 | 0.084 | 3.023 |
| Cobcroft and Battaglene [91] | 0.409 | 0.149 | 1.124 | 5.617 |
| Cobcroft and Battaglene [91] | 0.279 | 0.149 | 0.521 | 6.093 |
| Engrola et al. [92] | 1.245 | 0.681 | 2.275 | 6.115 |
| Faulk and Holt [93] | 0.024 | 0.001 | 0.407 | 3.000 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.835 | 5.102 |
| Fernández et al. [96] | 0.424 | 0.213 | 0.842 | 6.028 |
| Fernández et al. [96] | 0.174 | 0.086 | 0.352 | 6.011 |
| Opstad et al. [98] | 0.050 | 0.001 | 2.023 | 2.186 |
| Koumoundouros et al. [100] | 0.026 | 0.002 | 0.452 | 2.996 |
| Koumoundouros et al. [100] | 0.024 | 0.001 | 0.417 | 2.999 |
| Koumoundouros et al. [100] | 0.026 | 0.002 | 0.445 | 2.997 |
| *Head* | 0.212 | 0.079 | 0.569 | 31.056 |
| Olsvik et al. [73] | 0.192 | 0.100 | 0.370 | 11.596 |
| Sivaramakrishnan et al. [74] | 1.547 | 0.591 | 4.049 | 10.393 |
| Martins et al. [75] | 0.670 | 0.371 | 1.210 | 11.825 |
| Richard et al. [83] | 6.159 | 1.721 | 22.040 | 9.062 |
| Boglino et al. [87] | 0.881 | 0.461 | 1.683 | 11.628 |
| Hansen et al. [88] | 2.444 | 1.145 | 5.220 | 11.217 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.835 | 8.722 |
| Saavedra et al. [95] | 2.000 | 1.089 | 3.673 | 11.767 |
| Imsland et al. [97] | 3.871 | 1.233 | 12.150 | 9.621 |
| Cobcroft et al. [99] | 0.017 | 0.001 | 0.296 | 4.170 |
| *Skeletal* | 1.104 | 0.419 | 2.910 | 33.119 |
| Giebichenstein et al. [71] | 0.027 | 0.004 | 0.205 | 3.089 |
| Giebichenstein et al. [71] | 0.121 | 0.040 | 0.363 | 4.356 |
| Giebichenstein et al. [71] | 0.237 | 0.101 | 0.556 | 4.680 |
| Giebichenstein et al. [71] | 0.012 | 0.001 | 0.207 | 2.225 |
| Olsvik et al. [73] | 0.236 | 0.064 | 0.873 | 4.070 |
| Sivaramakrishnan et al. [74] | 1.547 | 0.591 | 4.049 | 4.543 |
| Martins et al. [75] | 0.670 | 0.371 | 1.210 | 4.964 |
| Iwasaki et al. [77] | 0.163 | 0.008 | 3.348 | 2.055 |
| Iwasaki et al. [77] | 0.019 | 0.001 | 0.317 | 2.218 |
| Iwasaki et al. [77] | 0.019 | 0.001 | 0.325 | 2.218 |
| Katan et al. [80] | 0.057 | 0.003 | 1.024 | 2.173 |
| Katan et al. [80] | 0.014 | 0.001 | 0.245 | 2.223 |
| Katan et al. [80] | 0.043 | 0.002 | 0.764 | 2.189 |
| Katan et al. [80] | 0.007 | 0.000 | 0.124 | 2.230 |
| Puvanendran et al. [81] | 0.699 | 0.129 | 3.773 | 3.543 |
| Puvanendran et al. [81] | 0.725 | 0.141 | 3.718 | 3.614 |
| Johannsdottir et al. [83] | 11.592 | 2.307 | 58.255 | 3.642 |
| Johannsdottir et al. [83] | 4.684 | 0.213 | 102.904 | 2.002 |
| Richard et al. [84] | 6.159 | 1.721 | 22.040 | 4.119 |
| Zouiten et al. [89] | 0.007 | 0.000 | 0.111 | 2.230 |
| Penglase et al. [90] | 0.963 | 0.503 | 1.844 | 4.906 |
| Cobcroft et al. [99] | 0.409 | 0.149 | 1.124 | 4.479 |
| Fernández et al. [17] | 0.094 | 0.020 | 0.457 | 3.695 |
| Nhu et al. [94] | 0.988 | 0.255 | 3.835 | 4.005 |
| Saavedra et al. [95] | 1.613 | 0.792 | 3.284 | 4.842 |
| Fernández et al. [17] | 0.463 | 0.224 | 0.956 | 4.827 |
| Nguyen et al. [16] | 1.671 | 0.951 | 2.937 | 4.989 |
| Imsland et al. [97] | 3.871 | 1.233 | 12.150 | 4.301 |
| Opstad et al. [98] | 0.050 | 0.001 | 2.023 | 1.575 |
| *Vertebra* | 0.359 | 0.169 | 0.761 | 35.824 |
| Combined effect size | 0.442 | 0.169 | 1.154 | |

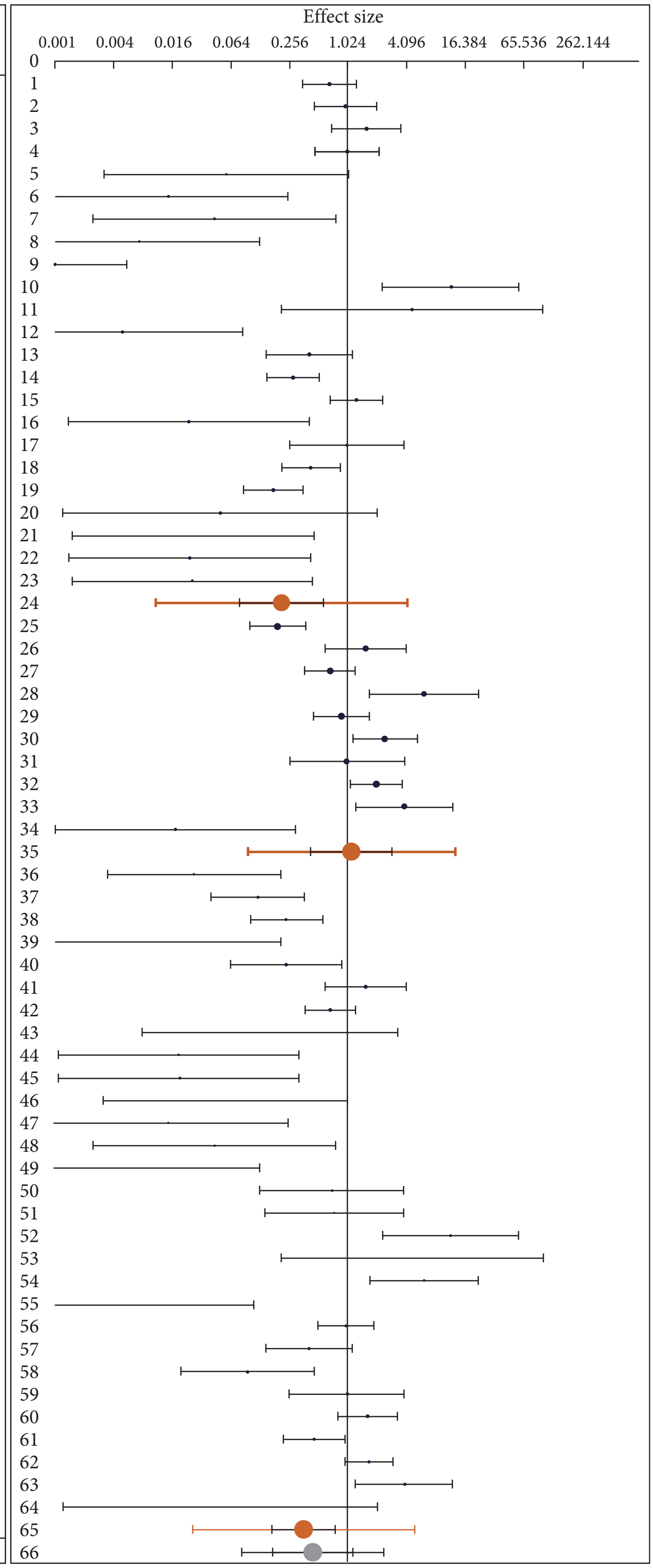



Figure 3: Forest plot diagram of the effect of deformation rate on deformation region/type.

Table 3: Meta-analysis results of deformation ratio of deformation region/type.

| Subgroup name | Odds ratio | CI lower limit | CI upper limit | Weight (%) | $Q$ | $p_Q$ | $I^2$ (%) | $T^2$ | $T$ | PI lower limit | PI upper limit |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Head | 0.21 | 0.08 | 0.57 | 31.06 | 154.40 | 0.001 | 85.75 | 1.82 | 1.35 | 0.01 | 4.11 |
| Vertebra | 0.36 | 0.17 | 0.76 | 35.82 | 147.27 | 0.001 | 80.99 | 1.51 | 1.23 | 0.03 | 4.96 |
| Skeletal | 1.10 | 0.42 | 2.91 | 33.12 | 59.01 | 0.001 | 84.75 | 0.99 | 0.99 | 0.10 | 12.77 |
| Combined effect size | 0.44 | 0.17 | 1.15 | | 379.96 | 0.001 | 83.95 | 1.47 | 1.21 | 0.08 | 2.35 |

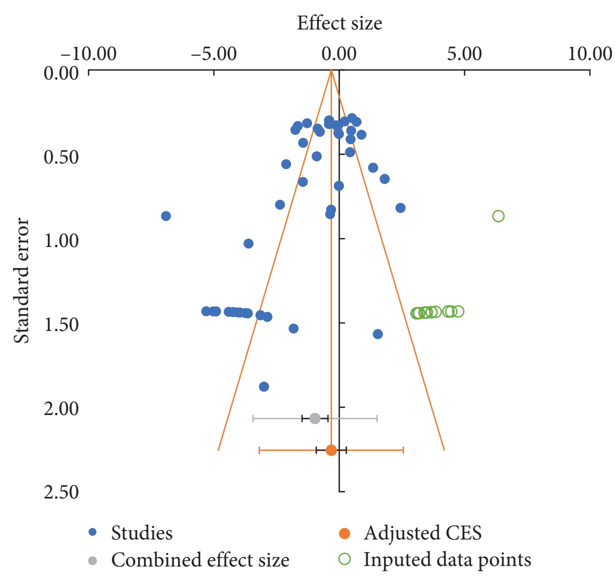



Figure 4: Funnel scatter plot (funnel pilot).

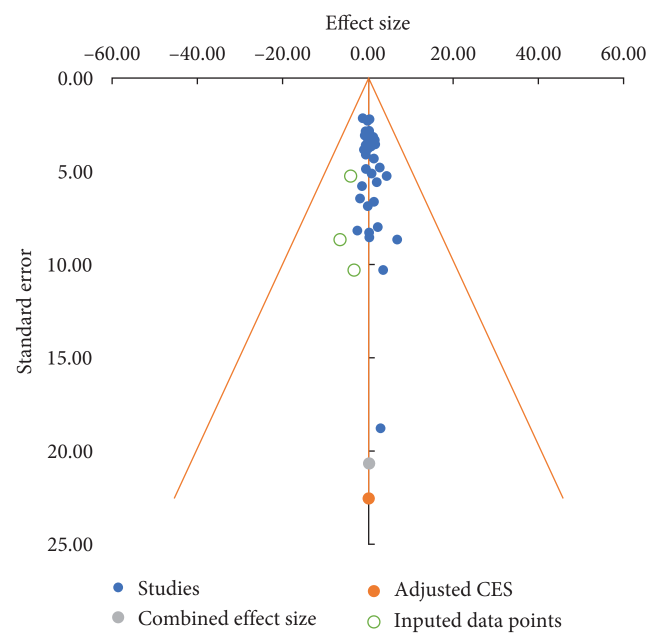



Figure 6: Funnel scatter plot for continent, agent, method, and phase (funnel pilot).

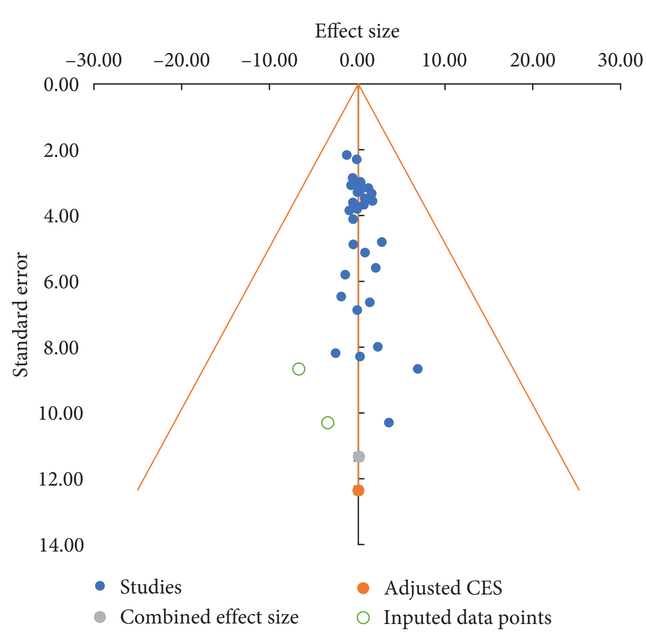



Figure 5: Funnel scatter plot for time (funnel pilot).

of the fish, different techniques are used to determine the intensity of deformation patterns and different degrees of accuracy. Deformations in fish can be detected by techniques such as external observation, X-ray, palpation, staining, synchrotron microcomputed tomography, computed tomography, histology, histopathology, histochemistry, and immunohistochemistry. These techniques may have some advantages and disadvantages depending on their application and/or larval age. More detailed applications are used in scientific studies, especially for larval stages. However, it has been shown that commercial companies confirm the quality standard by taking X-rays of a certain number of fish to register their quality at the sales stage, after sorting out the deformed fish at the appropriate stage.

So far, various factors have been shown to play a role in the development of skeletal abnormalities in different fish species under culture conditions. In general, skeletal abnormalities are thought to have significant adverse effects on animal welfare, biological performance of cultured fish, product quality, and production costs. Many of these explained factors indicate that, even if possible contaminants and pathogens in rearing conditions are controlled, improper feeding and/or starvation, adverse abiotic conditions, and genetic factors are the most likely causes of skeletal abnormalities in reared fish [51]. If nutritional requirements of preferred food are not met or more elements are supplied than necessary, especially during the early life development, this has a strong effect on skeletal deformities [123]. Proteins and amino

Table 4: Results of moderator analysis of studies with deformation in marine fish larvae farming.

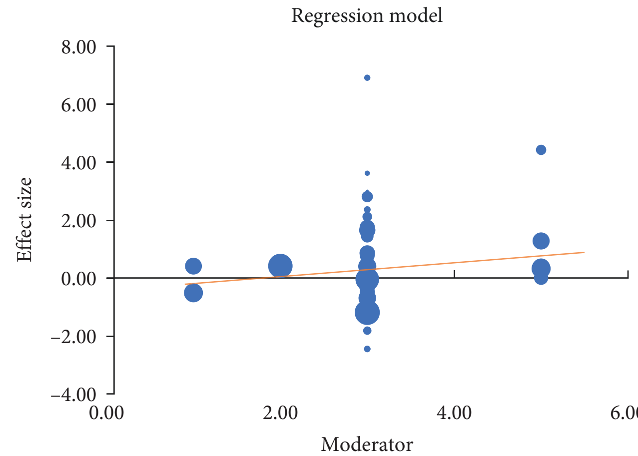
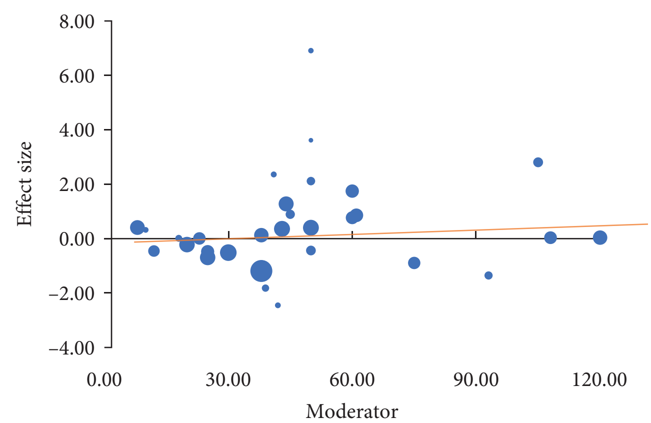
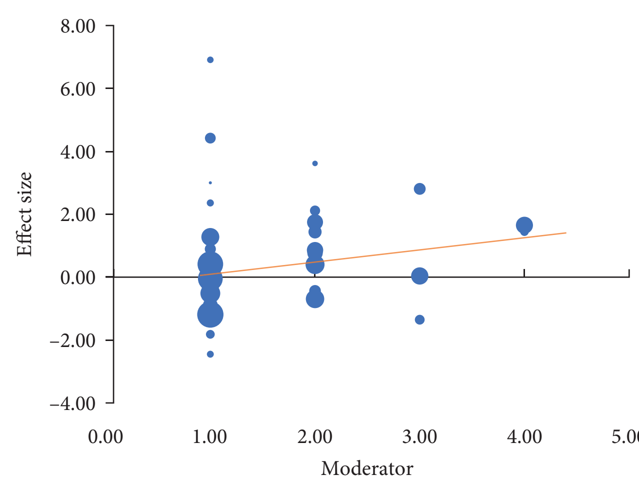
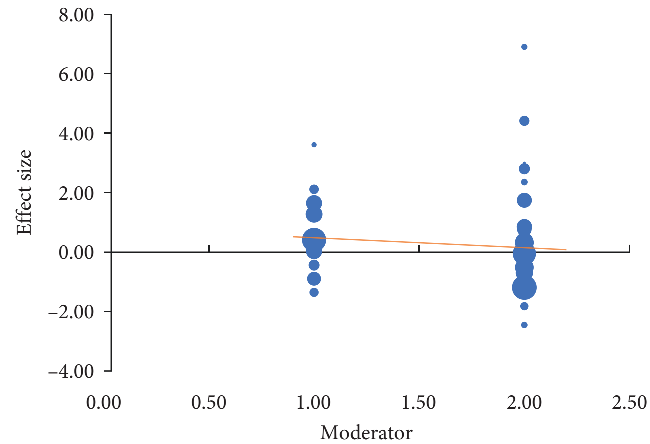
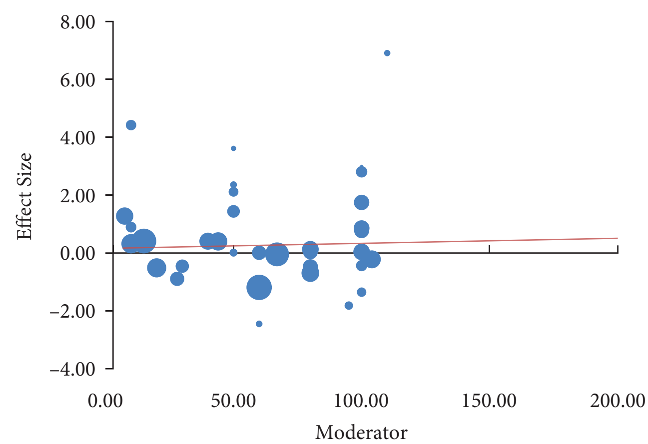
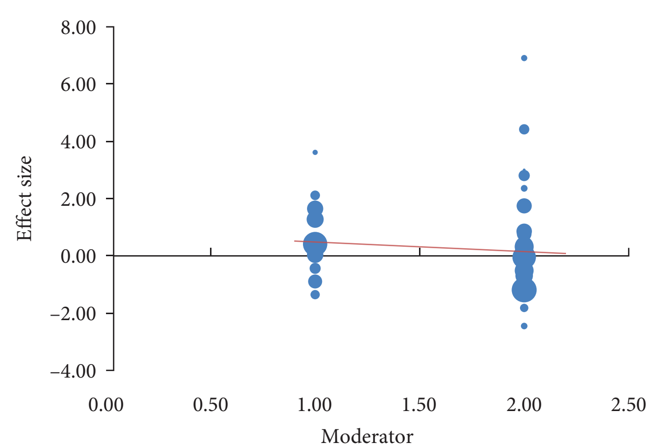
| Moderator | B | SE | 95% CI | $Z$-value | $p$-Value | Regression model |
|---|---|---|---|---|---|---|
| Region | 0.2390 | −0.88 | (1.36, 0.23) | 0.43 | 0.666 |  |
| Duration | −0.0971 | 0.0050 | (−2.02, 1.83) | −0.1027 | 0.9182 |  |
| Stage | 0.3869 | 0.74 | (−1.10, 1.88) | 0.53 | 0.599 |  |

Table 4: Continued.

| Moderator | B | SE | 95% CI | Z-value | p-Value | Regression model |
|---|---|---|---|---|---|---|
| Factor | −0.3349 | 1.22 | (−2.81, 2.14) | −0.27 | 0.784 |  |
| Stock density | 0.0017 | 0.0065 | (−0.0114) | 0.2706 | 0.7867 |  |
| Deformation analysis method | −0.3349 | 1.2210 | (−2.81, 2.14) | −0.2743 | 0.7839 |  |

acids, lipids and fatty acids (essential fatty acids, phospholipids, and oxidized lipids), and vitamins (water-soluble vitamins, fat-soluble vitamins, and minerals (macrominerals, trace elements) form the basis and content of feeds, and their effects on larvae are both it has been explained in detail in the form of a general assessment and the species in the review [51, 124]. On the other hand, the environmental factors most frequently cited as possible causes of skeletal abnormalities in reared fish are broodstock condition, egg quality, stocking density, rapid growth conditions, handling stress, hydrodynamic turbulence/water turbulence/water supply, rearing methods, light regime, mechanical factors, oil films on the water surface, $O_2/CO_2$ content, pH, physical trauma/mechanical stress, pathogens, parasites, toxins, radiation, salinity fluctuations, substrate condition (especially for flatfish), tank characteristics (volume, shape, color, and material), temperature fluctuations, antibiotics, and xenobiotics [13, 52, 59, 125–127]. In addition, genetic selection programs aimed at achieving rapid growth rates have been introduced over time; studies showing the inheritance of skeletal abnormalities, genetic drift, or gene mutations in deformed fish, their effects on phenotype, inbreeding, and selective breeding polyploidy were performed and interpreted [4, 34, 128–134].

The final success of the production is possible primarily by raising quality offspring. The most important precaution in this regard is to avoid sudden changes, keeping the physicochemical structure of the surrounding water under constant control at every stage of production and avoiding the factors that cause stress. In addition, it is important to obtain the broodstocks to be used in production from the natural environment, if possible, or to replace the population of broodstocks used in production with broodstocks obtained from nature at a certain rate (around 30%) every year. Feeding of broodstock with high-quality feed throughout the year or at least from the stage of egg formation will inevitably has a positive effect on the quality of the eggs. Fish eggs should be obtained in an environment free of pesticides, metal ions, hypochlorite, and other pollutants. Although it is not done most of the time, the bacterial load should be reduced by disinfecting the live eggs after the dead eggs are separated. Also, attention should be paid to egg stock density by hatching. In the larval period, it is important to prepare the environment of the tank according to the needs of the larvae (avoiding the formation of air bubbles, especially on the tank walls), to keep the stock density of the larvae optimal, and to avoid sudden changes in parameters and mechanical shocks. In particular, the influence of the light factor on the larval stage should not be forgotten. During this time, stress, especially from a sudden power outage, has a very strong effect on swimbladder hypertrophy. For this reason, the generator systems must be suddenly activated. In addition, sudden changes in salinity have a very strong effect on swimbladder hypertrophy during larval production in low salinity. Therefore, the sustainability of freshwater resources is important. Removal of the oil layer accumulated on the tank surface is inevitable for the formation of a functioning swimbladder. Surface cleaners should be placed according to the tank surface area and their cleaning should be done uninterruptedly. The flow rate applied to the tanks should be increased in direct proportion to the age of the larva, and the larva's swimming speed and resistance should be taken into consideration when making flow rate calculations. Automatic flow meters should be used in tanks. If the survival rate around day 20 in the tanks does not reach the desired level of quality larvae, the tanks should be quenched by chlorination. Chlorination is essential to maintain the natural population. Live food sources should be fortified with essential fatty acids and vitamins and refrigerated during the day, so they do not lose their nutritional value. In addition, the content of artificial feeds should be defined separately for each species, and the nutritional composition of the feeds should be determined for different developmental stages of the same species. In addition, before transferring the fish to net cages and/or earthen ponds for rearing, they should be examined on light tables for shape deformation, and deformed individuals should be separated and destroyed. In addition, it would be beneficial to follow the current literature and integrate all kinds of scientific data with the production system, to record the current production data system in a healthy way and to use these data in subsequent productions.

Despite these evaluations, which are considered a success for quality production, it is inevitable to encounter different problems at different stages of production, even when trying to meet all conditions. In a process where the survival rate under cultural conditions is so high compared to the natural environment, there will continue to be deformed individuals. Changes in deformation types and rates will inevitably affect ecosystem structure and function in the long run, as well as production, individuals escaping, or being released into the natural environment. The combination of degraded population structure in the natural environment with environmental impacts (especially microplastics and pollutants) poses a major threat to the ecological balance. There is no guarantee that this will not impact ecosystems and human communities.

This study examined 62 national and international studies on deformation rates between 1997 and 2022. The studies included in the study were identified by scanning Google Scholar, WOS, Scopus, Science Direct, and ULAKBİM data. In total, 100% of the national and international studies included in the study are covered within foreign articles. In this study, the meta-analysis method was used to analyze the studies on the topic of deformation "because it allows the results of many independent studies on a given topic to be combined and the findings obtained to be analyzed using statistical techniques." Unlike other screening methods, the meta-analysis method is based on numerical data and statistical techniques and provides a comprehensive and systematic summary of the literature on the studied concept [135].

Our results showed that the deformation rate had an overall negative effect on the functional properties of fish, regardless of the variables considered. The effect size appeared statistically significant and negative when analyzed as a whole, including all heterogeneous data. The number and content of the publications studied were determined to include the source of deformation. In addition, all statistically significant individual response variables had a negative effect size. Also in our study, the effects of deformation on region/type were supported by high $p$-values for maturity and stock density under the experimental conditions analyzed as a function of conditions in the variables considered. Therefore, the deformation publications showed that the deformation rate among the different subgroups was not affected by the continent, phase, factor, and moderators of the deformation detection method studied. In addition, it showed that the factor and the deformation detection method did not affect the effect size, and it was found that there was a strong change depending on the phase.

In this study, when the results were evaluated based on the meta-analysis method, it was found that the deformation rate was in the spine, head, and skeleton. In this regard, in the studies that were treated within the deformity region/type, 46% of the deformities were found in the spine, 37% in the head, and 16% in the skeleton. According to the meta-analysis results, the apparent value weight percentages were 35.82% in the spine, 33.12% in the skeleton, and 31.06% in the head.

Consequently, meta-analyzes may process results from multiple trials in aquaculture studies. However, results may differ between experimental conditions due to experimental conditions, parametric properties, and functional variability. Although meta-analysis is used in many fields, aquaculture is still developing. Meta-analysis of aquaculture studies also presents many challenges, including high heterogeneity, data sources, biased information, and nonautomated content of literature data. However, the findings from our global meta-analysis can be considered as a key indicator of deformities limiting fish production. In the future, advanced statistical tools such as Bayesian meta-analysis, network meta-analysis, and meta-regression analysis can be used to explore more complex data structures. The rapid development of artificial intelligence techniques will increase the efficiency of data collection and the robustness of results for meta-analysis studies in aquaculture and other fields.

## Data Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

## Disclosure

An earlier version of this work was published as a preprint by this team on Research Square: https://www.researchsquare.com/article/rs-3202114/v1 [136].

## Conflicts of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

## Authors' Contributions

All authors contributed to the study's conception and design. Hülya Eminçe Saygı contributed to conceptualization and writing—original draft. Hülya Eminçe Saygı, Hatice Tekoğul, Muammer Kürşat Fırat, Cüneyt Suzer, Osman Özden, and Fatih Güleç contributed to investigation. Hülya Eminçe Saygı and Muammer Kürşat Fırat contributed to methodology. Hülya Eminçe Saygı, Muammer Kürşat Fırat, Hatice Tekoğul, and Deniz Çoban contributed to supervision. Muammer Kürşat Fırat contributed to validation. Müge Aliye Hekimoğlu and Şahin Saka contributed to writing—review and editing. Şahin Saka contributed to visualization. Cüneyt Suzer, Osman Özden, Hatice Tekoğul, and Fatih Güleç contributed to resources. Deniz Çoban contributed to formal analysis. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. Each member of the author's team made a significant contribution to this study. All the authors are aware of and agree with the content of the manuscript.

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## References

[1] FAO, *The State of World Fisheries and Aquaculture. Sustainability in Action*, Food and Agriculture Organization of the United Nations, 2020.

[2] C. Daulas, A. N. Economou, and I. Bantavas, "Osteological abnormalities in laboratory reared sea bass (*Dicentrarchus labrax*) fingerlings," *Aquaculture*, vol. 97, no. 2-3, pp. 169–180, 1991.

[3] S. M. Scheiner, "Genetics and evolution of phenotypic plasticity," *Annual Review of Ecology and Systematics*, vol. 24, pp. 35–68, 1993.

[4] J. M. Afonso and F. J. Roo, "Anomalías morfológicas en peces cultivados: heredabilidad y selección," in *Genética y Genómica en Acuicultura*, pp. 215–240, CSIC, Madrid, 2007.

[5] S. Bolla and I. Holmefjord, "Effect of temperature and light on development of Atlantic halibut larvae," *Aquaculture*, vol. 74, no. 3-4, pp. 355–358, 1988.

[6] B. Chatain, "Abnormal swimbladder development and lordosis in sea bass (*Dicentrarchus labrax*) and sea bream (*Sparus auratus*)," *Aquaculture*, vol. 119, no. 4, pp. 371–379, 1994.

[7] G. Koumoundouros, F. Gagliardi, P. Divanach, C. Boglione, S. Cataudella, and M. Kentouri, "Normal and abnormal osteological development of caudal fin in *Sparus aurata* L. Fry," *Aquaculture*, vol. 149, no. 3-4, pp. 215–226, 1997.

[8] M. Kihara, S. Ogata, N. Kawano, I. Kubota, and R. Yamaguchi, "Lordosis induction in juvenile red sea bream, *Pagrus major*, by high swimming activity," *Aquaculture*, vol. 212, no. 1–4, pp. 149–158, 2002.

[9] M. Hattori, Y. Sawada, M. Kurata, S. Yamamoto, K. Kato, and H. Kumai, "Oxygen deficiency during somitogenesis causes centrum defects in red sea bream *Pagrus major* (Temminck et Schlegel)," *Aquaculture Research*, vol. 35, no. 9, pp. 850–858, 2004.

[10] P. G. Fjelldal, U. Nordgarden, A. Berg et al., "Vertebrae of the trunk and tail display different growth rates in response to photoperiod in Atlantic salmon, *Salmo salar* L., post-smolts," *Aquaculture*, vol. 250, no. 1-2, pp. 516–524, 2005.

[11] S. Elsadin, O. Nixon, N. Mozes et al., "The effect of dissolved carbon dioxide ($CO_2$) on white grouper (*Epinephelus aeneus*)

performance, swimbladder inflation and skeletal deformities," *Aquaculture*, vol. 486, pp. 81–89, 2018.

[12] C. Kitajima, T. Watanabe, Y. Tsukashima, and S. Fujita, "Lordotic deformation and abnormal development of swim bladders in some hatchery-bred marine physoclistous fish in Japan," *Journal of the World Aquaculture Society*, vol. 25, no. 1, pp. 64–77, 1994.

[13] C. Cahu, J. Zambonino Infante, and T. Takeuchi, "Nutritional components affecting skeletal development in fish larvae," *Aquaculture*, vol. 227, no. 1–4, pp. 245–258, 2003.

[14] S. J. Du and Y. Haga, "The zebrafish as a model for studying skeletal development," in *Biomineralization: Progress in Biology, Molecular Biology and Application*, E. Baeuerlein, Ed., pp. 283–304, Wiley-VCH, Weinheim, 2nd edition, 2004.

[15] S. P. Lall and L. M. Lewis-McCrea, "Role of nutrients in skeletal metabolism and pathology in fish—an overview," *Aquaculture*, vol. 267, no. 1–4, pp. 3–19, 2007.

[16] V. T. Nguyen, S. Satoh, Y. Haga, H. Fushimi, and T. Kotani, "Effects of zinc and manganese supplementation in *Artemia* on growth and vertebral deformity in red sea bream (*Pagrus major*) larvae," *Aquaculture*, vol. 285, no. 1–4, pp. 184–192, 2008.

[17] I. Fernández, M. S. Pimentel, J. B. Ortiz-Delgado et al., "Effect of dietary vitamin A on Senegalese sole (*Solea senegalensis*) skeletogenesis and larval quality," *Aquaculture*, vol. 295, no. 3-4, pp. 250–265, 2009.

[18] M. Saavedra, P. Pousão-Ferreira, M. Yúfera, M. T. Dinis, and L. E. C. Conceição, "A balanced amino acid diet improves *Diplodus sargus* larval quality and reduces nitrogen excretion," *Aquaculture Nutrition*, vol. 15, no. 5, pp. 517–524, 2009.

[19] M. Saavedra, L. E. C. Conceição, Y. Barr et al., "Tyrosine and phenylalanine supplementation on *Diplodus sargus* larvae: effect on growth and quality," *Aquaculture Research*, vol. 41, no. 10, pp. 1523–1532, 2010.

[20] M. J. Kingsford and C. A. Gray, "Influence of pollutants and oceanography on abundance and deformities of wild fish larvae," in *Detecting Ecological Impacts: Concepts and Applications in Coastal Habitats*, R. J. Schmitt and C. W. Osenberg, Eds., pp. 235–255, Academic Press, Osenberg New York, NY, 1996.

[21] M. Naruse, Y. Ishihara, S. Miyagawa-Tomita, A. Koyama, and H. Hagiwara, "3-Methylcholanthrene, which binds to the arylhydrocarbon receptor, inhibits proliferation and differentiation of osteoblasts in vitro and ossification in vivo," *Endocrinology*, vol. 143, no. 9, pp. 3575–3581, 2002.

[22] C. He, Z. Zuo, X. Shi et al., "Effects of benzo(a)pyrene on the skeletal development of *Sebastiscus marmoratus* embryos and the molecular mechanism involved," *Aquatic Toxicology*, vol. 101, no. 2, pp. 335–341, 2011.

[23] J. Corrales, C. Thornton, M. White, and K. L. Willett, "Multigenerational effects of benzo[a]pyrene exposure on survival and developmental deformities in zebrafish larvae," *Aquatic Toxicology*, vol. 148, pp. 16–26, 2014.

[24] F. Seemann, D. R. Peterson, P. E. Witten et al., "Insight into the transgenerational effect of benzo[a]pyrene on bone formation in a teleost fish (*Oryzias latipes*)," *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, vol. 178, pp. 60–67, 2015.

[25] S. Hodgson, L. Thomas, E. Fattore et al., "Bone mineral density changes in relation to environmental PCB exposure," *Environmental Health Perspectives*, vol. 116, no. 9, pp. 1162–1166, 2008.

[26] D. Carpi, M. Korkalainen, L. Airoldi et al., "Dioxin-sensitive proteins in differentiating osteoblasts: effects on bone formation in vitro," *Toxicological Sciences*, vol. 108, no. 2, pp. 330–343, 2009.

[27] M. Korkalainen, E. Kallio, A. Olkku et al., "Dioxins interfere with differentiation of osteoblasts and osteoclasts," *Bone*, vol. 44, no. 6, pp. 1134–1142, 2009.

[28] M. Herlin, F. Kalantari, N. Stern et al., "Quantitative characterization of changes in bone geometry, mineral density and biomechanical properties in two rat strains with different Ah-receptor structures after long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin," *Toxicology*, vol. 273, no. 1–3, pp. 1–11, 2010.

[29] J. Zhang, Z. Zuo, P. Sun, H. Wang, A. Yu, and C. Wang, "Tributyltin exposure results in craniofacial cartilage defects in rockfish (*Sebastiscus marmoratus*) embryos," *Marine Environmental Research*, vol. 77, pp. 6–11, 2012.

[30] B. Gjerde, M. J. R. Pante, and G. Baeverfjord, "Genetic variation for a vertebral deformity in Atlantic salmon (*Salmo salar*)," *Aquaculture*, vol. 244, no. 1–4, pp. 77–87, 2005.

[31] S. Ferraresso, M. Milan, C. Pellizzari et al., "Development of an oligo DNA microarray for the European sea bass and its application to expression profiling of jaw deformity," *BMC Genomics*, vol. 11, pp. 354–370, 2010.

[32] T. S. Silva, O. Cordeiro, N. Richard, L. E. C. Conceição, and P. M. Rodrigues, "Changes in the soluble bone proteome of reared white seabream (*Diplodus sargus*) with skeletal deformities," *Comparative Biochemistry and Physiology Part D: Genomics and Proteomics*, vol. 6, no. 1, pp. 82–91, 2011.

[33] D. Negrín-Báez, A. Navarro, J. M. Afonso, R. Ginés, and M. J. Zamorano, "Detection of QTL associated with three skeletal deformities in gilthead seabream (*Sparus aurata* L.): lordosis, vertebral fusion and jaw abnormality," *Aquaculture*, vol. 448, pp. 123–127, 2015.

[34] Á. Lorenzo-Felipe, H. S. Shin, S. León-Bernabeu et al., "The effect of the deformity genetic background of the breeders on the spawning quality of gilthead seabream (*Sparus aurata* L.)," *Frontiers in Marine Science*, vol. 8, Article ID 656901, 2021.

[35] F. Lagardere, M. Boulic, and T. Bürgin, "Anomalies in the cephalic area laboratory-reared larvae and juveniles of the common sole, *Solea solea*: jaws apparatus, dermal papillae and pigmentation," *Environmental Biology of Fishes*, vol. 36, pp. 35–46, 1993.

[36] A. Loy, S. Cataudella, and M. Corti, "Shape change of the sea bass, *D. labrax*, in relation to different rearing conditions; an analysis using Bookstein's shape co-ordinate and an application of the tinplate spleens regression analysis," in *Advances in Morphometrics*, N.A.T.O. ASI Series, pp. 399–406, Plenum Press, New York, 1996.

[37] C. Boglione, F. Gagliardi, M. Scardi, and S. Cataudella, "Skeletal descriptors and quality assessment in larvae and post-larvae of wild-caught and hatchery-reared gilthead sea bream (*Sparus aurata* L. 1758)," *Aquaculture*, vol. 192, no. 1, pp. 1–22, 2001.

[38] Y. Haga, T. Takeuchi, and T. Seikai, "Influence of all-trans retinoic acid on pigmentation and skeletal formation in larval Japanese flounder," *Fisheries Science*, vol. 68, no. 3, pp. 560–570, 2002.

[39] N. Nagano, A. Hozawa, W. Fuji et al., "Skeletal development and deformities in cultured larval and juvenile seven bond grouper, *Epinephelus septemfasciatus* (Thunberg)," *Aquaculture Research*, vol. 38, no. 2, pp. 121–130, 2007.

[40] I. Vågsholm and H. O. Djupvik, "Risk factors for spinal deformities in Atlantic salmon, *Salmo salar* L." *Journal of Fish Diseases*, vol. 21, no. 6, pp. 449–454, 1998.

[41] M. Hattori, Y. Sawada, Y. Takagi, R. Suzuki, T. Okada, and H. Kumai, "Vertebral deformities in cultured red sea bream, *Pagrus major*, Temminck and Schlegel," *Aquaculture Research*, vol. 34, no. 13, pp. 1129–1137, 2003.

[42] P. J. Gavaia, S. Domingues, S. Engrola et al., "Comparing skeletal development of wild and hatchery-reared Senegalese sole (*Solea senegalensis*, Kaup 1858): evaluation in larval and postlarval stages," *Aquaculture Research*, vol. 40, no. 14, pp. 1585–1593, 2009.

[43] M. H. Barahona-Fernandes, "Body deformation in hatchery reared European sea bass *Dicentrarchus labrax* (L.). Types, prevalence and effect on fish survival," *Journal of Fish Biology*, vol. 21, no. 3, pp. 239–249, 1982.

[44] M. Matsuoka, "Development of skeletal tissues and skeletal muscles in the red sea bream," *Bulletin of the Seikai Regional Fisheries Research Laboratory*, vol. 65, pp. 1–114, 1987.

[45] K. Hosoya and K. Kawamura, "Osteological evaluation in artificial seedling of *Paralichthys olivaceus* (Temminck and Schulegel)," pp. 107–114, 1991, UJNR Tech. Rept. 24.

[46] B. Glamuzina, B. Skaramuca, N. Glavić, and V. Kožul, "Preliminary studies on reproduction and early-stage rearing trial of dusky grouper, *Epinephelus marginatus* (Lowe, 1834)," *Aquaculture Research*, vol. 29, no. 10, pp. 769–771, 1998.

[47] S. Shiozawa, *II-4-(4) Health of Juvenile. In: Production Technique of Juvenile Yellowtail, Seriola quinqueradiata*, pp. 39–42, Fisheries Research Agency, Yokohama, Japan, 2006.

[48] E. Setiadi, S. Tsumura, D. Kassam, and K. Yamaoka, "Effect of saddleback syndrome and vertebral deformity on the body shape and size in hatchery-reared juvenile red spotted grouper, *Epinephelus akaara* (Perciformes: Serranidae): a geometric morphometric approach," *Journal of Applied Ichthyology*, vol. 22, no. 1, pp. 49–53, 2006.

[49] S. Pierre, S. Gaillard, N. Prevot-D'alvise et al., "Grouper aquaculture: Asian success and Mediterranean trials," *Aquatic Conservation: Marine and Freshwater Ecosystems*, vol. 18, no. 3, pp. 297–308, 2008.

[50] G. Koumoundouros, P. Divanach, and M. Kentouri, "The effect of rearing conditions on development of saddleback syndrome and caudal fin deformities in *Dentex dentex* (L.)," *Aquaculture*, vol. 200, no. 3-4, pp. 285–304, 2001.

[51] C. Boglione, E. Gisbert, P. Gavaia et al., "Skeletal anomalies in reared European fish larvae and juveniles. Part 2: main typologies, occurrences and causative factors," *Reviews in Aquaculture*, vol. 5, no. s1, pp. S121–S167, 2013.

[52] P. Divanach, C. Boglione, B. Menu, G. Koumoundouros, M. Kentouri, and S. Cataudella, "Abnormalities in finfish mariculture: an overview of the problem, causes and solutions," in *Handbook of Contributions and Short Communications, International Workshop on Sea Bass and Sea Bream Culture: Problems and Prospects*, pp. 45–66, Organized by European Aquaculture Society (EAS), Verona, Italy, 1996.

[53] L. Le Vay, G. R. Carvalho, E. T. Quinitio, J. H. Lebata, V. N. Ut, and H. Fushimi, "Quality of hatchery-reared juveniles for marine fisheries stock enhancement," *Aquaculture*, vol. 268, no. 1–4, pp. 169–180, 2007.

[54] J. Y. Park, K. H. Han, J. K. Cho, J. I. Myeong, and J. M. Park, "Early osteological development of larvae and juveniles in red spotted grouper, *Epinephelus akaara* (Pisces: Serranidae)," *Development & Reproduction*, vol. 20, no. 2, pp. 87–101, 2016.

[55] C. Boglione, G. Marino, M. Giganti, A. Longobardi, P. De Marzi, and S. Cataudella, "Skeletal anomalies in dusky grouper *Epinephelus marginatus* (Lowe 1834) juveniles reared with different methodologies and larval densities," *Aquaculture*, vol. 291, no. 1-2, pp. 48–60, 2009.

[56] E. Yamamoto, *Vertebral Fusion in Japanese Flounder Paralichthys olivaceus and Prevention. Text Book of 2008 Practical Course of Fish Farming Technology-Technical Approaches to Prevent Morphological Abnormality in Flounder Seed Production*, Japan Sea Farming Association, Tokyo, 2004.

[57] C. Olsen, E. Kjørsvik, A. I. Olsen, and K. Reitan, "Effect of different phospholipid sources and phospholipid: natural lipid value in formulated diets on larval deformities of Atlantic cod (*Gadus morhua*)," *Special Publication of European Aquaculture Society*, vol. 34, pp. 621-622, 2004.

[58] M.-H. Deschamps, A. Kacem, R. Ventura et al., "Assessment of "discreet" vertebral abnormalities, bone mineralization and bone compactness in farmed rainbow trout," *Aquaculture*, vol. 279, no. 1–4, pp. 11–17, 2008.

[59] G. Koumoundouros, "Morpho-anatomical abnormalities in mediterranean marine aquaculture," *Recent Advances in Aquaculture Research*, vol. 661, no. 2, pp. 125–148, 2010.

[60] A. M. de Azevedo, A. P. Losada, I. Ferreiro, A. Riaza, S. Vázquez, and M. I. Quiroga, "New insight on vertebral anomalies in cultured Senegalese sole (*Solea senegalensis*, Kaup) at early stages of development." *Journal of Fish Diseases*, vol. 40, no. 8, pp. 987–1000, 2017.

[61] J. M. Cobcroft and S. C. Battaglene, "Skeletal malformations in Australian marine finfish hatcheries," *Aquaculture*, vol. 396–399, pp. 51–58, 2013.

[62] T. D. S. Lopes, T. M. de Freitas, R. K. Jomori, D. J. Carneiro, and M. C. Portella, "Skeletal anomalies of pacu, *Piaractus mesopotamicus*, larvae from a wild-caught broodstock," *Journal of World Aquaculture Society*, vol. 45, no. 1, pp. 15–27, 2014.

[63] L. V. Hedges, "Meta-analysis," *Journal of Educational and Behavioral Statistics*, vol. 17, no. 4, pp. 279–296, 1992.

[64] R. Rosenthal and M. R. DiMatteo, "Meta-analysis: recent developments in quantitative methods for literature reviews," *Annual Review of Psychology*, vol. 52, no. 1, pp. 59–82, 2001.

[65] I. K. Crombie and H. T. O. Davies, *What is Meta-Analysis?*, Hayward Medical Communications, Fordham, 2009, http://anesthesia.mcmaster.ca/docs/librariesprovider17/defaultdocument-library/research-methodology/study-design-and-methodological-issues/what-is-meta-analysis.pdf?sfvrsn=23573363_0.

[66] M. Borenstein, L. V. Hedges, J. P. T. Higgins, and H. R. Rothstein, *Introduction to Meta-Analysis*, A John Wiley and Sons, Ltd., 2021.

[67] G. M. Tawfik, K. A. S. Dila, M. Y. F. Mohamed et al., "A step by step guide for conducting a systematic review and meta-analysis with simulation data," *Tropical Medicine and Health*, vol. 47, no. 1, Article ID 46, 2019.

[68] A. S. Pullin and G. B. Stewart, "Guidelines for systematic review in conservation and environmental management," *Conservation Biology*, vol. 20, no. 6, pp. 1647–1656, 2006.

[69] D. Moher, L. Shamseer, M. Clarke et al., "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement," *Systematic Reviews*, vol. 4, Article ID 1, 2015.

[70] N. Cozer, G. D. Pont, A. Horodesky, and A. Ostrensky, “Infrastructure, management and energy efficiency in a hypothetical semi-intensive shrimp model farm in Brazil: a systematic review and meta-analysis,” *Reviews in Aquaculture*, vol. 12, no. 2, pp. 1072–1089, 2020.

[71] J. Giebichenstein, J. Giebichenstein, M. Hasler, C. Schulz, and B. Ueberschär, “Comparing the performance of four commercial microdiets in an early weaning protocol for European seabass larvae (*Dicentrarchus labrax*),” *Aquaculture Research*, vol. 53, no. 2, pp. 544–558, 2022.

[72] Z. Fu, R. Yang, S. Zhou, Z. Ma, and T. Zhang, “Effects of rotifers enriched with different enhancement products on larval performance and jaw deformity of golden pompano larvae *Trachinotus ovatus* (Linnaeus, 1758),” *Frontiers in Marine Science*, vol. 7, Article ID 626071, 2021.

[73] P. A. Olsvik, E. Sørhus, S. Meier et al., “Ontogeny-specific skeletal deformities in atlantic haddock caused by larval oil exposure,” *Frontiers in Marine Science*, vol. 8, Article ID 726828, 2021.

[74] T. Sivaramakrishnan, K. Ambasankar, K. P. Kumaraguru Vasagam et al., “Effect of dietary soy lecithin inclusion levels on growth, feed utilization, fatty acid profile, deformity and survival of milkfish (*Chanos chanos*) larvae,” *Aquaculture Research*, vol. 52, no. 11, pp. 5366–5374, 2021.

[75] G. Martins, L. Ribeiro, A. Candeias-Mendes et al., “Reduction of skeletal anomalies in meagre (*Argyrosomus regius*, Asso, 1801) through early introduction of inert diet,” *Aquaculture Research*, vol. 50, no. 10, pp. 2782–2792, 2019.

[76] Ø. J. Hansen, V. Puvanendran, J. P. Jøstensen, and I. B. Falk-Petersen, “Early introduction of an inert diet and unenriched *Artemia* enhances growth and quality of Atlantic cod (*Gadus morhua*) larvae,” *Aquaculture Nutrition*, vol. 24, no. 1, pp. 102–111, 2018.

[77] T. Iwasaki, N. Inoue, K. Teruya, and K. Hamasaki, “Osteological development and deformities in hatchery-reared longtooth grouper (*Epinephelus bruneus*): vertebral column, dorsal-fin supports and caudal-fin skeleton,” *Aquaculture Research*, vol. 49, no. 10, pp. 3245–3257, 2018.

[78] S. Zhou, J. Hu, R. Yang, and Z. Ma, “Effects of live food enrichment on yellowtail amberjack *Seriola lalandi dorsalis* (Gill 1863) larvae,” *Israeli Journal of Aquaculture–Bamidgeh*, vol. 70, 2018.

[79] G. J. Partridge and L. D. Woolley, “The performance of larval *Seriola lalandi* (Valenciennes, 1833) is affected by the taurine content of the *Artemia* on which they are fed,” *Aquaculture Research*, vol. 48, no. 3, pp. 1260–1268, 2017.

[80] T. Katan, G. W. Nash, M. L. Rise et al., “A little goes a long way: improved growth in Atlantic cod (*Gadus morhua*) fed small amounts of wild zooplankton,” *Aquaculture*, vol. 451, pp. 271–282, 2016.

[81] V. Puvanendran, I.-B. Falk-Petersen, H. Lysne, H. Tveiten, H. Toften, and S. Peruzzi, “Effects of different step-wise temperature increment regimes during egg incubation of Atlantic cod (*Gadus morhua* L.) on egg viability and newly hatched larval quality,” *Aquaculture Research*, vol. 46, no. 1, pp. 226–235, 2015.

[82] A. Boglino, M. J. Darias, J. B. Ortiz-Delgado et al., “Commercial products for *Artemia* enrichment affect growth performance, digestive system maturation, ossification, and incidence of skeletal deformities in Senegalese sole (*Solea senegalensis*) larvae,” *Aquaculture*, vol. 324-325, pp. 290–302, 2012.

[83] J. Johannsdottir, H. L. Heimisdottir, K. Hakonardottir et al., “Improved performance of Atlantic cod (*Gadus morhua* L.) larvae following enhancement of live feed using a fish protein hydrolysate,” *Aquaculture Nutrition*, vol. 20, no. 3, pp. 314–323, 2014.

[84] N. Richard, I. Fernández, T. Wulff et al., “Dietary supplementation with vitamin k affects transcriptome and proteome of senegalese sole, improving larval performance and quality,” *Marine Biotechnology (New York, NY)*, vol. 16, no. 5, pp. 522–537, 2014.

[85] A. Skalli, J.-L. Zambonino-Infante, Y. Kotzamanis, R. Fabregat, and E. Gisbert, “Peptide molecular weight distribution of soluble protein fraction affects growth performance and quality in European sea bass (*Dicentrarchus labrax*) larvae,” *Aquaculture Nutrition*, vol. 20, no. 2, pp. 118–131, 2014.

[86] R. K. Negm, J. M. Cobcroft, M. R. Brown, B. F. Nowak, and S. C. Battaglene, “The effects of dietary vitamin A in rotifers on the performance and skeletal abnormality of striped trumpeter *Latris lineata* larvae and post larvae,” *Aquaculture*, vol. 404–405, pp. 105–115, 2013.

[87] L. Prestinicola, C. Boglione, P. Makridis et al., “Environmental conditioning of skeletal anomalies typology and frequency in gilthead seabream (*Sparus aurata* L., 1758) juveniles,” *PLoS ONE*, vol. 8, no. 2, Article ID e55736, 2013.

[88] Ø. J. Hansen, V. Puvanendran, J. P. Jøstensen, and C. Ous, “Effects of dietary levels and ratio of phosphatidylcholine and phosphatidylinositol on the growth, survival and deformity levels of Atlantic cod larvae and early juveniles,” *Aquaculture Research*, vol. 42, no. 7, pp. 1026–1033, 2011.

[89] D. Zouiten, I. Ben Khemis, A. Slaheddin Masmoudi, C. Huelvan, and C. Cahu, “Comparison of growth, digestive system maturation and skeletal development in sea bass larvae reared in an intensive or a mesocosm system,” *Aquaculture Research*, vol. 42, no. 11, pp. 1723–1736, 2011.

[90] S. Penglase, A. Nordgreen, T. van der Meeren et al., “Increasing the level of selenium in rotifers (*Brachionus plicatilis* “Cayman”) enhances the mRNA expression and activity of glutathione peroxidase in cod (*Gadus morhua* L.) larvae,” *Aquaculture*, vol. 306, no. 1–4, pp. 259–269, 2010.

[91] J. M. Cobcroft and S. C. Battaglene, “Jaw malformation in striped trumpeter *Latris lineata* larvae linked to walling behaviour and tank colour,” *Aquaculture*, vol. 289, no. 3-4, pp. 274–282, 2009.

[92] S. Engrola, L. Figueira, L. E. C. Conceição, P. J. Gavaia, L. Ribeiro, and M. T. Dinis, “Co-feeding in *Senegalese sole* larvae with inert diet from mouth opening promotes growth at weaning,” *Aquaculture*, vol. 288, no. 3-4, pp. 264–272, 2009.

[93] C. K. Faulk and G. J. Holt, “Early weaning of southern flounder, *Paralichthys lethostigma*, larvae and ontogeny of selected digestive enzymes,” *Aquaculture*, vol. 296, no. 3-4, pp. 213–218, 2009.

[94] V. C. Nhu, K. Dierckens, T. H. Nguyen, M. T. Tran, and P. Sorgeloos, “Can umbrella-stage *Artemia franciscana* substitute enriched rotifers for Cobia (*Rachycentron canadum*) fish larvae?” *Aquaculture*, vol. 289, no. 1-2, pp. 64–69, 2009.

[95] M. Saavedra, Y. Barr, P. Pousao-Ferreira et al., “Supplementation of tryptophan and lysine in *Diplodus sargus* larval diet: effects on growth and skeletal deformities,” *Aquaculture Research*, vol. 40, no. 10, pp. 1191–1201, 2009.

[96] I. Fernández, F. Hontoria, J. B. Ortiz-Delgado et al., "Larval performance and skeletal deformities in farmed gilthead sea bream (*Sparus aurata*) fed with graded levels of vitamin A enriched rotifers (*Brachionus plicatilis*)," *Aquaculture*, vol. 283, no. 1–4, pp. 102–115, 2008.

[97] A. K. Imsland, A. Foss, R. Koedijk, A. Folkvord, S. O. Stefansson, and T. M. Jonassen, "Short-and long-term differences in growth, feed conversion efficiency and deformities in juvenile Atlantic cod (*Gadus morhua*) startfed on rotifers or zooplankton," *Aquaculture Research*, vol. 37, no. 10, pp. 1015–1027, 2006.

[98] I. Opstad, J. Suontama, E. Langmyhr, and R. E. Olsen, "Growth, survival, and development of Atlantic cod (*Gadus morhua* L.) weaned onto diets containing various sources of marine protein," *ICES Journal of Marine Science*, vol. 63, no. 2, pp. 320–325, 2006.

[99] J. M. Cobcroft, P. M. Pankhurst, C. Poortenaar, B. Hickman, and M. Tait, "Jaw malformation in cultured yellowtail kingfish (*Seriola lalandi*) larvae," *New Zealand Journal of Marine and Freshwater Research*, vol. 38, no. 1, pp. 67–71, 2004.

[100] G. Koumoundouros, G. Oran, P. Divanach, S. Stefanakis, and M. Kentouri, "The opercular complex deformity in intensive gilthead sea bream (*Sparus aurata* L.) larviculture. Moment of apparition and description," *Aquaculture*, vol. 156, no. 1-2, pp. 165–177, 1997.

[101] J. J. Deeks, "Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes," *Statistics in Medicine*, vol. 21, no. 11, pp. 1575–1600, 2002.

[102] E. Schechtman, "Odds ratio, relative risk, absolute risk reduction, and the number needed to treat—Which of these should we use?" *Value in Health*, vol. 5, no. 5, pp. 431–436, 2002.

[103] S. Dinçer, "Applied meta-analysis in educational sciences (in Turkish)," p. 133, Pegem Atıf İndeksi, 2014.

[104] J. Cohen, "Set correlation and contingency tables," *Applied Psychological Measurement*, vol. 12, no. 4, pp. 425–434, 1988.

[105] P. D. Ellis, *The Essential Guide to Effect Sizes: Statistical Power, Meta-Analysis, and the Interpretation of Research Results*, Cambridge University Press, 2010.

[106] H. Van Rhee, R. Suurmond, and T. Hak, "User manual for meta-essentials: workbooks for meta-analysis," Available at SSRN 3241355, 2015.

[107] R. Suurmond, H. van Rhee, and T. Hak, "Introduction, comparison, and validation of meta-essentials: a free and simple tool for meta-analysis," *Research Synthesis Methods*, vol. 8, no. 4, pp. 537–553, 2017.

[108] M. Borenstein, "Effect sizes for continuous data," in *The Handbook of Research Synthesis and Meta-Analysis*, H. Cooper, L. V. Hedges, and J. C. Valentine, Eds., pp. 221–235, Russell Sage Foundation, 2009.

[109] M. D. Higgins, R. J. Green, and M. S. Leeson, "Optical wireless for intra vehicle communications: a channel viability analysis," *IEEE Transactions on Vehicular Technology*, vol. 61, no. 1, pp. 123–129, 2012.

[110] M. Borenstein, L. V. Hedges, J. P. T. Higgins, and H. R. Rothstein, "Meta-analize giriş," in *Introduction to Meta-Analysis*, Wiley, Anı Yayıncılık, Ankara (in Turkish), Article ID 416, 2013.

[111] C. B. Begg and M. Mazumdar, "Operating characteristics of a rank correlation test for publication bias," *Biometrics*, vol. 50, no. 4, pp. 1088–1101, 1994.

[112] R. M. Harbord and P. Whiting, "Metandi: meta-analysis of diagnostic accuracy using hierarchical logistic regression," *The Stata Journal*, vol. 9, no. 2, pp. 211–229, 2009.

[113] T. S. Avery, S. S. Killen, and T. R. Hollinger, "The relationship of embryonic development, mortality, hatching success, and larval quality to normal or abnormal early embryonic cleavage in Atlantic cod, *Gadus morhua*," *Aquaculture*, vol. 289, no. 3-4, pp. 265–273, 2009.

[114] O. J. Hansen and V. Puvanendran, "Fertilization success and blastomere morphology as predictors of egg and juvenile quality for domesticated Atlantic cod, *Gadus morhua*, broodstock," *Aquaculture Research*, vol. 41, no. 12, pp. 1791–1798, 2010.

[115] A. J. Trotter, P. M. Pankhurst, and S. C. Battaglene, "Morphological development of the swim bladder in hatchery-reared striped trumpeter *Latris lineata*," *Journal of Applied Ichthyology*, vol. 20, no. 5, pp. 395–401, 2004.

[116] L. D. Woolley and J. G. Qin, "Swimbladder inflation and its implication to the culture of marine finfish larvae," *Reviews in Aquaculture*, vol. 2, no. 4, pp. 181–190, 2010.

[117] S. Grotmol, H. Kryvi, and G. K. Totland, "Deformation of the notochord by pressure from the swim bladder may cause malformation of the vertebral column in cultured Atlantic cod *Gadus morhua* larvae: a case study," *Diseases of Aquatic Organisms*, vol. 65, no. 2, pp. 121–128, 2005.

[118] C. Boglione, G. Marino, A. Fusari, F. Ferreri, M. G. Finoia, and S. Cataudella, "Skeletal anomalies in *Dicentrarchus labrax* juveniles selected for functional swimbladder," *ICES Marine Science Symposium*, vol. 201, pp. 163–169, 1995.

[119] J. A. Andrades, J. Becerra, and P. Fernandez-Llebrez, "Skeletal deformities in larval, juvenile, and adult stages of cultured gilthead sea bream (*Sparus aurata* L.)," *Aquaculture*, vol. 141, no. 1-2, pp. 1–11, 1996.

[120] Y. Sawada, M. Hattori, N. Sudo et al., "Hypoxic conditions induce centrum defects in red sea bream *Pagrus major* (Temminck and Schlegel)," *Aquaculture Research*, vol. 37, no. 8, pp. 805–812, 2006.

[121] N. Komada, "Incidence of gross malformations and vertebral anomalies of natural and hatchery *Plecoglossus altivelis*," *Copeia*, vol. 1980, no. 1, pp. 29–35, 1980.

[122] P. G. Fjelldal, T. J. Hansen, and A. E. Berg, "A radiological study on the development of vertebral deformities in cultured Atlantic salmon (*Salmo salar* L.)," *Aquaculture*, vol. 273, no. 4, pp. 721–728, 2007.

[123] I. Rønnestad, M. Yúfera, B. Ueberschär, L. Ribeiro, Ø. Sæle, and C. Boglione, "Feeding behavior and digestive physiology in larval fish: current knowledge, and gaps and bottlenecks in research," *Reviews in Aquaculture*, vol. 5, no. s1, pp. S59–S98, 2013.

[124] K. Hamre, M. Yúfera, I. Rønnestad, C. Boglione, L. E. C. Conceição, and M. Izquierdo, "Fish larval nutrition and feed formulation: knowledge gaps and bottlenecks for advances in larval rearing," *Reviews in Aquaculture*, vol. 5, no. s1, pp. S26–S58, 2013.

[125] J. L. Zambonino-Infante and C. L. Cahu, "Effect of nutrition on marine fish development and quality," in *Recent Advances in Aquaculture Research*, G. Koumoundouros, Ed., pp. 103–124, Transworld Research Network, Kerala, India, 2010.

[126] E. Georgakopoulou, P. Katharios, P. Divanach, and G. Koumoundouros, "Effect of temperature on the development of skeletal deformities in Gilthead seabream (*Sparus aurata* Linnaeus, 1758)," *Aquaculture*, vol. 308, no. 1-2, pp. 13–19, 2010.

[127] C. Boglione and C. Costa, "Skeletal deformities and juvenile quality," in *Sparidae: Biology and Aquaculture of Gilthead Sea Bream and Other Species*, M. A. Pavlidis and C. C. Mylonas, Eds., pp. 233–294, John Wiley & Sons, Ltd., Oxford, 2011.

[128] J. Castro, A. Pino-Querido, M. Hermida et al., "Heritability of skeleton abnormalities (lordosis, lack of operculum) in gilthead seabream (*Sparus aurata*) supported by microsatellite family data," *Aquaculture*, vol. 279, no. 1–4, pp. 18–22, 2008.

[129] A. Navarro, M. J. Zamorano, S. Hildebrandt, R. Ginés, C. Aguilera, and J. M. Afonso, "Estimates of heritabilities and genetic correlations for growth and carcass traits in gilthead seabream (*Sparus auratus* L.), under industrial conditions," *Aquaculture*, vol. 289, no. 3-4, pp. 225–230, 2009.

[130] J. M. Cobcroft, A. C. Shu-Chien, M.-K. Kuah, A. Jaya-Ram, and S. C. Battaglene, "The effects of tank colour, live food enrichment and green water on the early onset of jaw malformation in striped trumpeter larvae," *Aquaculture*, vol. 356–357, pp. 61–72, 2012.

[131] E. Gisbert, A. Skalli, I. Fernández, Y. Kotzamanis, J. L. Zambonino-Infante, and R. Fabregat, "Protein hydrolysates from yeast and pig blood as alternative raw materials in microdiets for gilthead sea bream (*Sparus aurata*) larvae," *Aquaculture*, vol. 338–341, pp. 96–104, 2012.

[132] H. G. Park, V. Puvanendran, A. Kellett, C. C. Parrish, and J. A. Brown, "Effect of enriched rotifers on growth, survival, and composition of larval Atlantic cod (*Gadus morhua*)," *ICES Journal of Marine Science*, vol. 63, no. 2, pp. 285–295, 2006.

[133] D. G. Sfakianakis, E. Georgakopoulou, I. E. Papadakis, P. Divanach, M. Kentouri, and G. Koumoundouros, "Environmental determinants of haemal lordosis in European sea bass, *Dicentrarchus labrax* (Linnaeus, 1758)," *Aquaculture*, vol. 254, no. 1–4, pp. 54–64, 2006.

[134] T. Takeuchi, J. Dedi, Y. Haga, T. Seikai, and T. Watanabe, "Effect of vitamin A compounds on bone deformity in larval Japanese flounder (*Paralichthys olivaceus*)," *Aquaculture*, vol. 169, no. 3-4, pp. 155–165, 1998.

[135] I. Kasarci, *The effectiveness of project based learning on students' academic achievements and attitude: a meta-analysis*, p. 109, Osman Gazi University, Eskisehir, Unpublished Master thesis, 2013

[136] H. Eminçe Saygı, M. K. Fırat, M. A. Hekimoğlu et al., "Meta-analysis of the causality of deformations in marine fish larvae culture," 2023.