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Changes of blood cholinesterase activities among pesticides-exposed agricultural workers in Iraq: A meta-analysis

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ABSTRACT

Numerous studies in Iraq have attempted to determine blood cholinesterase (ChE) activities with varying results in agricultural workers and veterinarians exposed to pesticides. This meta-analysis answers the specific inquiry of whether or not blood ChE activities decrease in agricultural workers exposed previously to pesticides. The meta-analysis included 14 records of blood ChE activities extracted from 12 studies after employing the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). These records comprised ChE activities in agricultural workers exposed to pesticides (n = 635) versus their respective control cohorts (n = 416). We employed the one-group random effects model for the meta-analysis and the Newcastle–Ottawa Scale (NOS) to examine study quality. The combined effect size of pesticides exposed group (% ChE activity versus control) was significant at 86.13 %. Heterogeneity (I^2 = 49.86 %) was moderate. Subgroup analysis of the enzyme source (plasma/serum and erythrocytes/whole blood) revealed that plasma effect size was significant at 82.36 % compared to erythrocytes (92.08 %), which was not significant. No publication bias existed. The studies were of high quality (NOS ≥ 7). The present study is the first meta-analytic report of associating reduced blood ChE activities with pesticides exposure in Iraqi agricultural workers. Reduced pseudo ChE (plasma, serum) activity was the most significant indicator of pesticides exposure. Nevertheless, we recommend biomonitoring erythrocyte and even whole blood ChE activities in pesticides-exposed individuals, because of scarce information on the type and frequency of pesticides employed by Iraqi agricultural workers. Our findings call for a national integrated plan and improved regulations for safer and judicious pesticides applications and follow-up practices in Iraq in order to reduce potential health hazards and environmental risks.

1. Introduction

Pesticides are extensively used globally, including developing countries, in agriculture and crop production, general hygiene and veterinary medicine with considerable health and environmental impacts [1–5]. According to pests targeted to be controlled or eradicated, pesticides mainly include herbicides, fungicides, biocides, rodenticides, molluscicides, nematicides, insecticides, pediculocides and plant growth regulators [1,4–6]. It is estimated that worldwide annual production of pesticides exceeds three billion kilograms [7]. Due to the wide and unregulated usage of pesticides, they became environmental contaminants as well as a threat to human and animal health by causing unintentional acute toxicity crises or chronic poisoning issues such as cancers, neurological disorders, chemical sensitivity, or reproductive adverse effects [1–5,8–14]. Additionally, pesticides exposure has been linked to draining economic resources, increasing health costs and causing damages to the ecosystem and biodiversity [15–18]. The impact of pesticides is even worse in developing countries because of heavy use and uncontrolled management of these compounds [2,19–22].

Within the agricultural sector such as that of Iraq and as found elsewhere, the category of agricultural workers and laborers mainly include farmers, crews of agricultural production, harvesting,

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greenhouses, florists, forestry, gardens, plant nursery and agricultural facilities, as well as engineers, veterinarian and those tending livestock and animal production [2,6,23,24]. As pesticides could be misused and applied injudiciously, workers at the agricultural sector could be susceptible to their toxic effects [1–3,7,20,21,24,25]. To this end, numerous studies have shown the usage of pesticides in Iraq with their potential adverse health effects and environmental impacts [26–36].

As pesticides gain access to the body via oral, dermal and inhalational routes, determination of plasma (serum) or erythrocyte (ChE) activities is a useful monitoring tool to judge exposure of individuals (e.g. farmers) to pesticides, particularly organophosphates and carbamates [1,3,4,8,19,24,37–39].The plasma ChE (EC 3.1.1.8) is also named as pseudo ChE, which is secreted by the liver, whereas those of the brain and erythrocytes are the true ChE (EC 3.1.1.7) [39–41]. Hence, the enzyme of erythrocytes reflects the status of neuronal ChE activity [41,42]. Further, these two enzymes are differently inhibited by various ChE inhibiting pesticides and regenerate at different rates, being the erythrocyte ChE the slow one [41–44]. To this end, pesticides exposure is suggested when any blood ChE activity is reduced by 20–30 % from the predetermined baseline value, and subsequently the individual should be removed from the exposure condition when the serum ChE activity falls to ≥40 % of baseline value [41–44]. A ChE inhibition by ≥50 % confirms the anti-ChE exposure and poisoning and thus hospitalization might be needed [41–44]. However, 10.6 % decrease in blood ChE activity was found to be significant in farmer chronically exposed to pesticides [37].

As blood ChE activities are monitored globally to assess exposure of agricultural workers to pesticides [37–44], several studies in Iraq have attempted to determine plasma and/or erythrocyte ChE activity in order to monitor exposure of farmworkers and veterinarians to pesticides, but with varying results [33,36,45–50].These were in the form of significant [33,36,45–49] or even non-significant [49,50] reductions in at least one of the blood ChE activities. It was unfortunate that the majority of Iraqi studies did not confirm the type of pesticide to which exposure have occurred; even the extent of exposure and its frequency were not reported [36,45]. Iraqi studies, lacking systematic evaluation, have reported decreases of ChE activity in the plasma, erythrocytes, or the whole blood of agricultural labors and veterinarians that ranged as 8.1 %-38.1 % in Mosul [45,46], 10 %-44.5 % in Erbil [33,47], 22 % in Kirkuk [48], 0 %-15 % in Duhok [49,50] and 54 % in Baghdad [36]. Unfortunately, other studies on pesticides exposure in Iraq did not report blood ChE activities at all [31–35]. Furthermore, no systematic review and meta-analysis were conducted to evaluate biomonitoring dilemma of pesticides exposure among agricultural workers in Iraq.

Since Iraq lacks a national ChE monitoring program in agricultural workers, it is quite difficult to evaluate and interpret ChE inhibition in pesticides-exposed individuals in the absence of pre-exposure enzyme levels [50–53]. In the light of uncertainty of the type of pesticide exposure and its level in Iraqi agricultural workers and the variability or even inconsistency in the results of ChE biomonitoring, it became pertinent to employ a meta-analysis to answer specifically whether or not blood ChE activities decrease in agricultural workers exposed previously to pesticides.

2. Materials and methods

2.1. Approval

The Scientific Reviewing Board, Department of Pharmacology, College of Pharmacy at the University of Duhok, Iraq has approved to conduct this meta-analysis. The present meta-analysis did not involve any direct human subject participation, as the analysis was on data retrieved from published literature.

2.2. Study duration and location

The current meta-analysis was started from conceptualization March 3, 2024 till the end of analysis and drafting the manuscript on September 20, 2024 at the College of Pharmacy, University of Duhok, Duhok, Kurdistan Region, Iraq.

2.3. Search strategy

The following data bases were searched: Iraqi Academic Scientific Journals (IACSJ), Iraqi Digital Repository for Theses and Dissertations, Pubmed, Google Scholars, Scopus (Science Direct), Directory of Open Access Journals (DOAJ) and Web of Science My Research Assistant till September 20, 2024. The search strings included the following key words/phrases: “cholinesterase” or “acetylcholinesterase” or “Iraq” or “blood (plasma, serum, or erythrocytes) cholinesterase” and “pesticides” or “insecticides” or “organophosphates” or “carbamates”; “human cholinesterase + Iraq” or “pesticides + Iraq + cholinesterase” or “farmers + Iraq + pesticides” or “Iraq + cholinesterase” or “agricultural workers + cholinesterase + Iraq” or “agricultural workers + pesticides + Iraq. Additionally search included citations of published articles chosen for the current meta-analysis. No language restriction was imposed on searching strategy. All authors participated in searching the data bases.

2.4. Inclusion criteria

Study selection for the meta-analysis was according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [54] (Fig. 1). We selected published studies that specifically reported values as means ± standard deviation (SD) or standard error (SE) of blood (serum, plasma, erythrocytes or whole blood) ChE activities in Iraqi agricultural workers (including veterinarians) who had the history of previous exposure to pesticides during their routine work in the agriculture sector versus their control cohorts. Initial literature search identified 310 studies according to key words/phrases mentioned above. The final records for the present meta-analysis included were 14 that were extracted from 8 studies regardless of the occurrence of changes in ChE activity or not (Fig. 1, Table 1). As shown in Table 1, study records comprised ChE activities of plasma/serum (n = 9), erythrocytes (n = 4) and whole blood (n =1).

2.5. Exclusion criteria

Studies not reporting blood ChE activity of agriculture workers or veterinarians in Iraq were excluded from the present meta-analysis. Theses and dissertations that showed duplicate records were also excluded. Any issue arose concerning inclusion and exclusion of studies, or extracting ChE activity values was solved by discussion and subsequent agreement with the reviewer FKM.

2.6. Data extraction and handling

All the reviewers (FKM, AAM and SKO) used the key words and phrases mentioned above to search the data bases. Blood (plasma, serum, erythrocyte or whole blood) ChE activities of Iraqi agricultural workers exposed to pesticides were extracted from figures and tables or texts of selected articles depending on the inclusion and exclusion criteria. The records were tabulated as shown in Table 1 to include authors and year of publication, number of subjects, ChE activity in the plasma, serum, erythrocytes or whole blood (mean ± SD unit of enzyme activity) of pesticides exposed agricultural workers and their control counterparts. Different methods (e.g. spectrophotometric and electrometric) were applied to determine blood ChE activities that resulted in ChE values with various units of measurements (Table 1). Therefore, for the present meta-analysis, we unified the mean ± SD of ChE activities of pesticides-exposed group as the percentage of its corresponding control

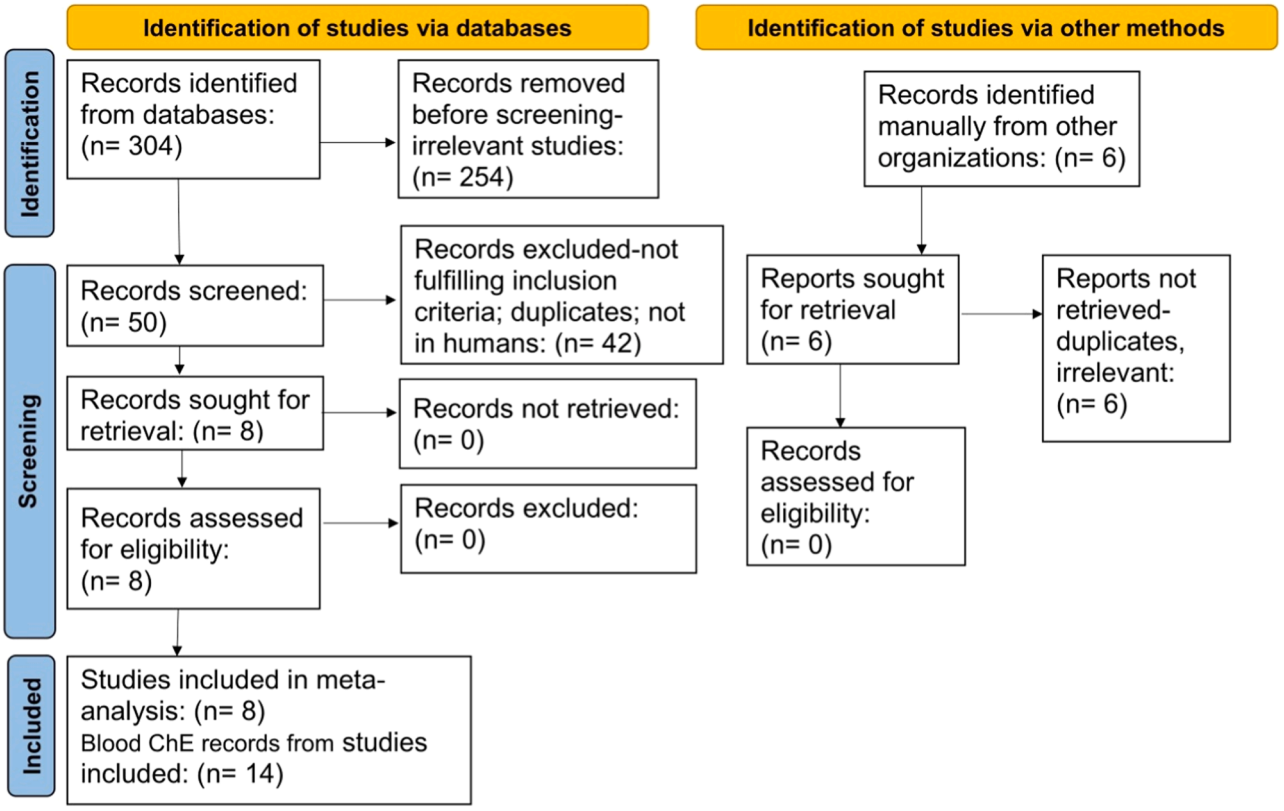

Fig. 1. Application of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) to select studies reporting blood cholinesterase (ChE) activities of agricultural workers exposed to pesticides.

Table 1
Changes in blood cholinesterase activities in pesticides exposed agricultural workers in Iraq.

Authors [reference No.]	Code	ChE	ChE activity unit	Mean control ChE ± SD	n	Mean exposed ChE ± SD	n	% of control ± SD
Ahmed and Mohammad [45]	A	Plasma	Δ pH/20 min	1.05 ± 0.153	40	0.65 ± 0.171	6	61.90 ± 16.286
	B	RBC	Δ pH/20 min	1.18 ± 0.127	45	0.87 ± 0.220	6	73.73 ± 18.644
Ahmed and Mohammad [46]	C	Plasma	Δ pH/20 min	1.05 ± 0.153	40	0.966 ± 0.204	36	92.00 ± 19.429
	D	RBC	Δ pH/20 min	1.18 ± 0.127	45	1.084 ± 0.155	36	91.864 ± 13.136
Al-Haseni and Yahya [47]	E	Plasma	Δ pH/20 min	0.93 ± 0.04	50	0.74 ± 0.07	31	95.57 ± 7.527
	F	Plasma	Δ pH/20 min	0.93 ± 0.04	50	0.83 ± 0.07	67	89.25 ± 7.527
	G	Plasma	Δ pH/20 min	0.93 ± 0.04	50	0.84 ± 0.07	76	90.32 ± 7.527
Ahmed [48]	H	Whole blood	Δ pH/20 min	1.44 ± 0.14	12	1.12 ± 0.13	40	77.78 ± 9.028
Othman and Kaky [33]	I	Serum	ng/ml	12.08 ± 2.634	21	6.705 ± 2.815	75	55.50 ± 23.303
Mohammed and Mohammad [49]	J	Plasma	Δ pH/20 min	1.491 ± 0.155	15	1.286 ± 0.101	15	86.25 ± 6.774
	K	RBC	Δ pH/20 min	1.082 ± 0.039	15	1.042 ± 0.058	15	96. 303 ± 5.360
Odisho and Mohammad [50]	L	Plasma	Δ pH/20 min	1.10 ± 0.195	44	1.07 ± 0.192	92	97.27 ± 17.45
	M	RBC	Δ pH/20 min	1.38 ± 0.141	44	1.39 ± 0.101	92	100.72 ± 7.32
Abdulsalam et al. [36]	N	Serum	U/L	95.00 ± 16.02	30	43.77 ± 11.22	90	46.07 ± 11.81

value. When ChE activity was reported as mean and range of minimum to maximum values, the SD was calculated according to Wan et al. [55]. The final analysis encompassed 14 records of % mean ± SD blood ChE activities in pesticides exposed Iraqi agricultural workers (versus respective controls).

2.7. Statistical analysis

We used Meta-Essentials, Version 1.5 (Erasmus Research Institute of Management, Rotterdam, Netherlands) [56] to conduct randomized effects size one-arm meta-analysis on blood ChE activities of pesticides exposed Iraqi agricultural workers. The meta-analysis included forest and funnel plots, and estimation of effect size with 95 % confidence intervals (C.I.), weight of each record, statistical Z-test at p value of < 0.05, as well as heterogeneity analysis [56,57].

2.8. Heterogeneity analysis

The meta-analysis software mentioned above considers the potential heterogeneity of the results [56]. According, we assessed the heterogeneity of the meta-analysis results statistically by the Cochrane *Q*-test at a p value of < 0.10, in addition to the calculated $I^{\hat{}2}$ value that may range as 0 % (no heterogeneity) to 100 % (high level of heterogeneity) [56–59]. Depending on the results of heterogeneity analysis, which comprised a moderate level of heterogeneity, additional subgroup analysis was conducted on blood ChE activities based on two groups of the enzyme [56,57]. These groups were the pseudo ChE in the plasma/serum and the true one in erythrocytes/whole blood (mainly true ChE) of pesticides-exposed Iraqi agricultural workers. Pseudo and true ChEs are known to differ in their kinetics and extent of inhibition and the susceptibility to ChE inhibiting pesticides [39–43,60].

2.9. Publication bias

Publication bias, as depicted by the funnel plot of the effect size against the standard error was constructed by the software tool, and it was visually examined. In addition, results of the statistical procedure Egger's regression test at $p < 0.05$ are usually employed to confirm the presence of any publication bias [59,61].

2.10. Quality of the studies

All studies selected for the present meta-analysis were subjected to quality evaluation by the Newcastle–Ottawa Scale (NOS) [62]. Briefly, each study was scored using the NOS to assess three quality variables which were categorized into selection (4 stars), comparability (2 stars) and exposure (3 stars) with an optimum quality score being nine, and five or less as indicative of low quality (high risk of bias) [62]. Two reviewers independently applied the NOS to score studies of the present meta-analysis in order to detect risk of bias in a particular study [62]. Thereafter, the final scoring was accomplished collectively by all the reviewers.

3. Results

3.1. Searching and extraction of data records

The use of PRISMA flow chart (Fig. 1) depicts the identification, screening and selection of studies that included records of blood ChE activities in the plasma, serum, erythrocytes or the whole blood of pesticides-exposed agricultural workers in comparison with their respective controls. Data search using key words/phrases mentioned before retrieved 310 studies. After applying inclusion and exclusion criteria, the final number of records selected for the present meta-analysis was 14 belonging to eight studies extracted from literature, which were published articles between 2004 and 2024 (Fig. 1, Table 1). These records comprised ChE activity of the plasma (n = 7), serum (n = 2), erythrocytes (n = 4) and whole blood (n = 1) in agricultural workers exposed to pesticides (n = 635 samples) versus their respective control cohorts (n = 416 samples).

3.2. Meta-analysis

The combined effect size (% ChE activity) of pesticides exposed group versus control as shown by the forest plot was 86.13 % with a standard error = 4.03 and 95 % C.I. lower and upper limits = 77.42 and 94.84, respectively. The overall decrease (13.87 %) in blood ChE activities of pesticides exposed agricultural workers from those of the controls was significant at Z = 21.36, two-tailed p value = 0.0001 (Fig. 2). This inhibition of enzyme activity most probably reflects potential antiChE properties of pesticides such as organophosphates and carbamates [8,39,41,60]. Weights of study records varied from 2.27 % to 12.38 % (Fig. 2).

3.3. Heterogeneity analysis

The index of heterogeneity (I^2) of the analyzed data was 49.86 %, with corresponding T^2 and T values of 87.04 and 9.33, respectively; suggesting a moderate level of data heterogeneity, but significant as indicated by the Cochrane *Q* statistical test yielding *Q* of 25.93 at p = 0.017.

3.4. Subgroup analysis

Although the heterogeneity of the data appeared to be within the low-moderate range, (I^2 = 49.86 %; pseudo R^2 value = 12.21 %), subgroup analysis according to source of the enzyme (plasma/serum and erythrocytes/whole blood) revealed that plasma effect size was significant at 82.36 % (95 % C.I.= 68.8, 95.9) with a heterogeneity index (I^2) of 55.37 % (*Q* = 17.92, p = 0.022), in comparison to that of erythrocytes (92.08 %, 95 % C.I.= 79.25, 105.0 %) which was not significant at I^2 = 26.06 % (*Q* = 5.41, p = 0.248) (Fig. 3). To this end, from this subgroup analysis it appeared that pseudo ChE (plasma, serum) was the most significant contributor to the reduction in blood ChE activity in pesticides exposed agricultural workers with a weight of 43.07 % versus that of the true ChE of erythrocytes/whole blood (56.93 %).

3.5. Publication bias observed by the funnel plot

The funnel plot of the data points depicting SE versus effect size did not show publication bias within the appointed area of the plot, and the trim-and-fill analysis did not predict imputed points (Fig. 4). Additional

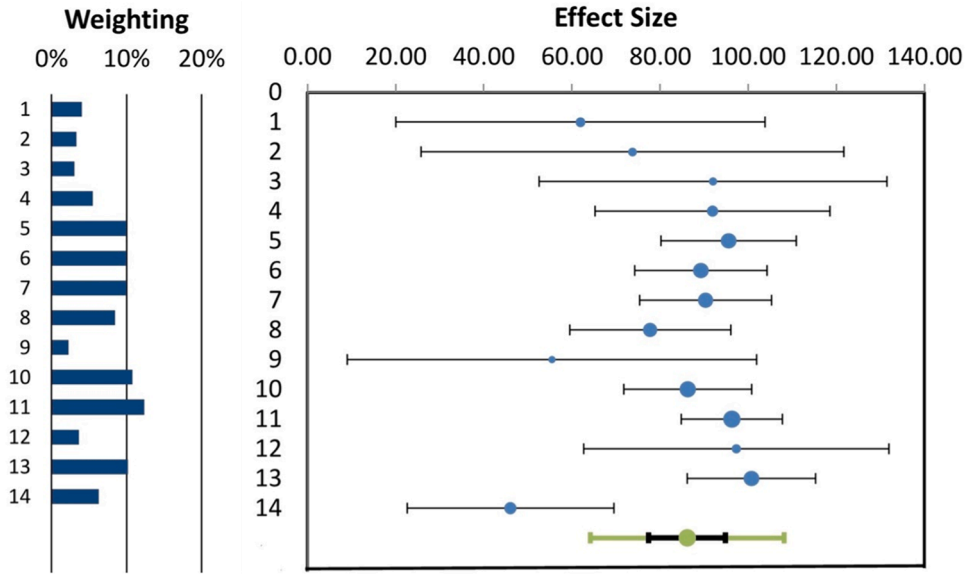

Fig. 2. Forest plot of blood cholinesterase activities and their comparative weightings in agricultural workers exposed to pesticides. Effect sizes were represented as percentages of respective control values.

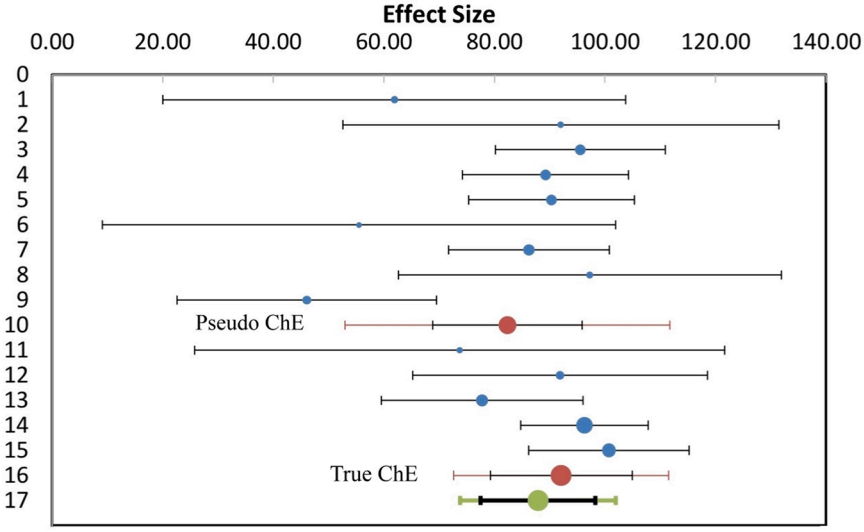

Fig. 3. Forest plot of subgroup analysis of pseudo (plasma/serum) and true (erythrocytes/whole blood) cholinesterase (ChE) activities in agricultural workers exposed to pesticides.

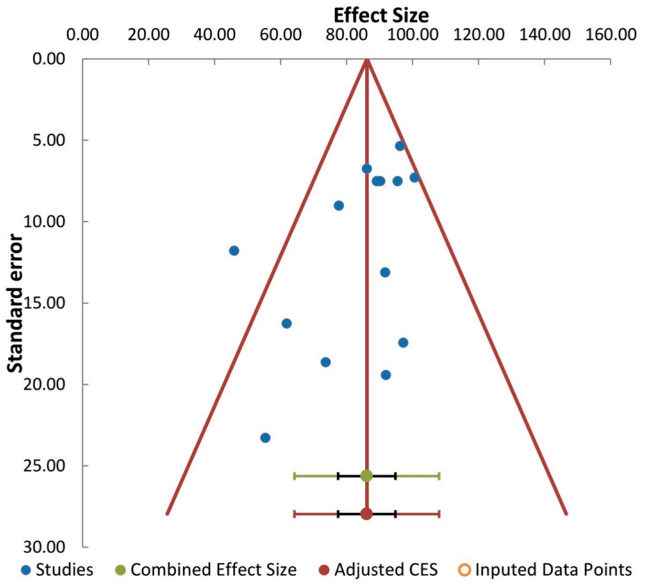

Fig. 4. Funnel plot to observe publication bias of blood cholinesterase activities of agricultural workers exposed to pesticides.

confirmation of no publication bias came from the results of the Egger's regression analysis which was not statistically significant (t = −1.80, p = 0.0.097).

3.6. Quality of studies

Examining the total NOS scores of the eight studies indicated that they were of high quality (NOS ≥ 7), with a median score of 7.0, ranging between 7 and 8 (Table 2). After subjecting the NOS scores of the eight studies to one-group proportions meta-analysis (Fig. 5), the resultant forest plot produced a standardized proportion mean (95 % C.I.) of 0.81 (0.70, 0.89) with no heterogeneity ($Q = 1.36$; $p = 0.987$; $I^2 = 0$ %)

4. Discussion

The decrease in blood ChE activities is a biomarker and indicative of prior exposure to organophosphate or carbamate pesticides [37–42].

Table 2
The use of Newcastle–Ottawa Scale (NOS) to assess the risk of bias scores of studies included in the meta-analysis.

Author [reference No.]	Criteria								Total NOS score
	Selection				Comparability	Exposure			
	1	2	3	4	**	1	2	3	9
	*	*	*	*		*	*	*	
Ahmed and Mohammad [45]	*	*	*	*	*	*	*	-	7
Ahmed and Mohammad [46]	*	*	*	*	*	*	*	-	7
Al-Haseni and Yahya [47]	*	*	*	*	*	*	*	-	7
Ahmed [48]	*	*	*	*	*	*	*	-	7
Othman and Kaky [33]	*	*	*	*	*	*	**	-	8
Mohammed and Mohammad [49]	*	*	*	*	*	*	*	-	7
Odisho and Mohammad [50]	*	*	*	*	*	*	**	-	8
Abdulsalam et al. [36]	*	*	*	*	*	*	**	-	8

High study quality is indicated when NOS ≥ 7.
* =Yes

Ranges of decline in blood ChE activities vary considerably according to the type of pesticide used, the extent of exposure and its frequency and whether or not personal protective equipment (PPE) are used during pesticides preparation and application [38–44]. As the Iraqi market place is prospering with various pesticides (including ChE inhibiting pesticides), which can be obtained easily, it is eminent that unintentional exposure to pesticides would occur [25,26,32,34–36,50]. This is especially true since pesticides are heavily used in Iraq without restrictions and agricultural workers/pesticides handlers mostly do not employ PPE [25,26,32,34–36,50].

The weight of the records of the present study ranged from 2.27 % to 12.38 % with significant, but moderate heterogeneity ($I^2 = 49.86$ %). Based on these findings, subsequent subgroup analysis showed that the

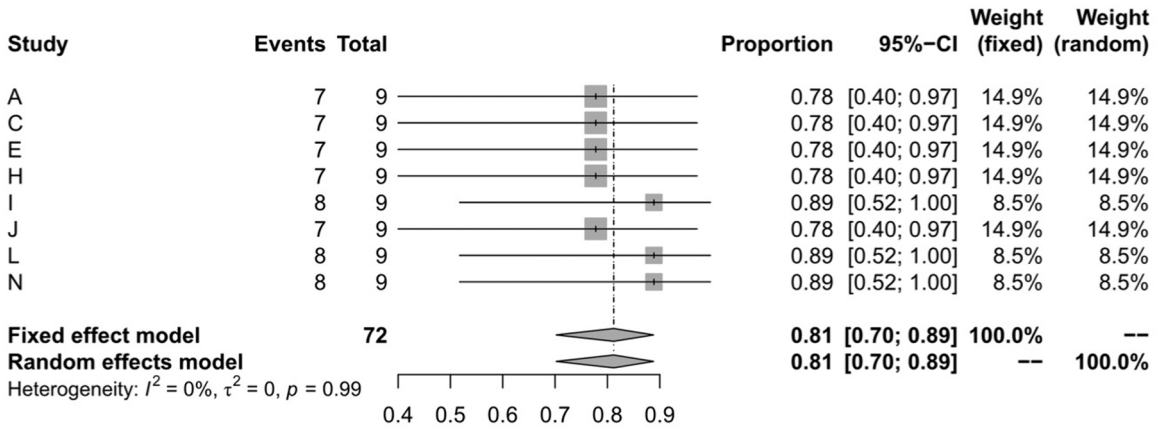

Fig. 5. Forest plot of the Newcastle–Ottawa Scale (NOS) scores of studies involving blood cholinesterase activities of agricultural workers exposed to pesticides. High study quality is indicated when NOS $\geq$ 7.

effect size of pseudo ChE activity in the plasma/serum subgroup (82.36 %) was significant, whereas that of the true ChE in erythrocytes/whole blood subgroup (92.08 %) was not. To this end, the present meta-analysis demonstrated that overall significant reduction in pseudo ChE activity was by 17.64 %, regardless of the types of pesticides used, which were largely unknown or not reported at all [36,45–50]. The erythrocyte ChE activity was non-significantly reduced by only 7.92 %. This could be associated among other factors with the differential ChE inhibition by pesticides or the chronicity of exposure to low levels of pesticides in the absence of acute episodes of overt poisoning [8,37,39–45,60]. In addition, considering the mechanism of toxicity, some pesticides such as organophosphates inhibit the ChE activity irreversibly with a rather slow recovery pattern, whereas carbamates cause reversible enzyme inhibition with a relatively rapid regeneration process [8,40,41,60].

Based on the current findings, plasma/serum ChE activity was a better indicator of pesticides exposure among the studies of the present met-analysis. This notion coincides with those of others in advocating plasma ChE as an earlier biomarker of pesticides exposure among agricultural workers [28–33]. However, this does not negate measuring the erythrocyte ChE activity, as others prefer this biomonitoring assay since it mirrors the biological and toxicological impact of pesticides on the CNS, and hence separate measurements of pseudo and true ChE activities facilitate a better pesticides exposure evaluation [28–33].

From the present results, we did not observe any publication bias within the designated area of the funnel plot, which was also supported by the insignificant Egger's regression analysis (p = 0.0.097). Furthermore, the studies were of high quality based on the NOS scoring system and the resultant forest plot (standardized proportion mean = 0.81) with no heterogeneity.

Pesticides are of utmost importance in controlling pest-related diseases, providing food security and subsequent advances in economic development [5,20,23]. They are widely applied in agriculture, veterinary clinical practice and public health sector [1–5] However, in spite of these benefits, there are immediate and long term health hazards as well as adverse impacts on the biodiversity, and ecosystem in association with pesticides uses, especially when applied injudiciously [1–3,13–18, 22]. To this end, our findings, showing reduced pseudo ChE activity among agricultural workers exposed to pesticides, call for a national integrated plan and improved regulations for safer and judicious pesticides uses and monitoring with enforced follow-up practices in Iraq in order to reduce potential health hazards and environmental risks [3–5,8, 15,16]. Considering these points, there is a definite need for implementing stricter national regulations on dispensing pesticides and their uses together with improved protection measures and periodic blood ChE monitoring programs.

Based on the findings of the current meta-analysis (reduced ChE activity) and those of other international studies [39,42–44] as well as some Iraqi studies, though lacking meta-analyses [36,45–51], we recommend measuring both pseudo and true ChE activities in agricultural workers exposed to pesticides, especially in absence of supporting data or evidence on the type of pesticides used, its duration and frequency of exposure. Even the whole blood ChE activity could be measured when field conditions preclude immediate separation of plasma aliquots [42,63]. However, many factors affect the level of ChE activity in blood components of pesticides exposed workers. These include bot not limited to the variability of pseudo and true ChEs in susceptibility to pesticide inhibition, type and intrinsic toxic activity of individual pesticide in use, dietary habit, age, gender and body weight of the worker, the use of PPE, combined pesticides usage which might lead to additive or synergistic toxicity, as well as the amount of the pesticide exposed to, its duration of exposure and frequency of exposure [2–4,19, 22,38,39,42,43,60,63].

It is also possible to evaluate pesticides hazard by analyzing the odds and risk ratios of occurrence of 20 % and more decrease in blood (usually plasma) ChE activity among agricultural workers [50,64]. In the absence of baseline ChE values of Iraqi agricultural workers [50–53], and the undefined pesticides type or usage mode, it is conceivable to call for establishing a national program to assess blood ChE activities of agricultural workers as well as handlers of pesticides, before and periodically after pesticides applications, with proper documentations regarding their types and usage modes.

5. Limitations and future directions

Most of the studies used for the current meta-analysis have not reported the type and frequency of pesticides applied by agricultural workers with or without PPE. No confounders were reported by studies of the present meta-analysis that would have affected blood ChE activities. The determination of blood ChE activities and units of measurements were not the same across the studies. This was corrected by analyzing the percentages of ChE activity of pesticides-exposed workers versus control (Table 1). It is critical to address in future studies potential impact of unmeasured confounders, such as socioeconomic factors, dietary habits, as well as concurrent disease conditions like uncontrolled diabetes mellitus, respiratory diseases and cardiovascular ailments when biomonitoring blood ChE activities among agricultural workers who use pesticides. Additional studies are needed to investigate and biomonitoring long-term health consequences of pesticides exposure and the effectiveness of interventions to reduce exposure and its adverse impacts.

6. Conclusion

The present study is the first meta-analytic report of associating reduced blood ChE activities with pesticides exposure in Iraqi agricultural workers. Reduced pseudo ChE (plasma, serum) activity was the most contributor to the reduction in blood ChE activities of pesticides exposed agricultural workers. Nevertheless, we recommend biomonitoring erythrocyte and even whole blood ChE activities in pesticides-exposed individuals, because of scarce information on the type and frequency of pesticides employed by Iraqi agricultural workers. A national Iraqi program would be in place for the assessment of blood ChE activities in agricultural workers to establish baseline values and judging workplace entry or removal. Under such a national program, it is essential to undertake several precautionary measures for Iraqi agricultural workers subjected to periodic measurements of blood ChE activities. These would include among other measures, documenting the types of pesticides used, its concentration and method of application, the use of PPE, frequency of exposure, as well as cost-benefit effects of any pesticide application taking into account the impacts on public health, ecosystem and biodiversity.

Ethical approval and consent to participate

Not applicable.

Ethical responsibilities of authors

All authors have read, understood, and complied as applicable with the statement on "Ethical responsibilities of Authors" as found in the Instructions for Authors.

Funding

Not Applicable.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Simona K. Odisho: Writing – review & editing, Visualization, Validation, Methodology, Data curation. **Fouad Kasim Mohammad:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ammar A. Mohammed:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data Availability

Data will be made available on request.

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