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Biochemical Parameters of Laboratory Animals in Iraq: A Meta-analysis Study

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A B S T R A C T

Our objective in this work was to estimate normal values of biochemical parameters in laboratory animals in Iraq. Values were pooled from studies conducted in Iraqi universities using a meta-analysis approach. Pertinent peer-reviewed published studies were retrieved from the Iraqi Academic Scientific Journals (IASJ) database. Random-effects inverse-variance model was used to obtain pooled means of the parameters from the set of studies qualified for the analysis. Among a total of 460 records identified from IASJ, 264 records were eligible for the statistical analysis, which reported 102 values for different biochemical parameters. The mean of the sample size for normal animals that was used in the studies including in the analysis were 8, 8, and 6 for rats, mice, and rabbits respectively. The mean ± standard deviation of ages (months) was 2.8 ± 1.0, 3.14 ± 1.15, and 9.2 ± 3.3 for rats, mice, and rabbits respectively. In this analysis, we estimated 31, 14, and 15 parameters from 121, 41, and 26 studies of rats, mice, and rabbits correspondingly. The proportion of variance in the parameters for the analyzed studies due to heterogeneity was significant. Evidence of bias in the estimated values due to small studies was found in some parameters. In conclusion, we encourage researchers to consider the values we provided in this analysis and report details of the sample size, number of animals in each group, sex, exact age, and the accurate units for the estimated values in their studies to facilitate further analyses for more reference values in further analyses.

Keywords: normal values, rats, mice, rabbits, meta-analysis

INTRODUCTION

Laboratory animals are extensively used in different studies in Iraqi universities as those for the global use, particularly in the experimental studies of physiology, biochemistry, pharmacology, and toxicology. Taylor and Alvarez (1) reported the use of 192.1 million animals in scientific research in 142 countries worldwide during 2015, including 79.9 million animals for scientific procedure purposes. The authors indicated that there was a 36.6% increase in the number of laboratory animals used for scientific research compared to the year 2005. Among all laboratory animals, rats and mice are considered the most common species used in the research. These animals can be housed in a small space and characterized by rapid reproduction with a short life span that allows studying consecutive generations (2). To provide a statistic about the number of rats and mice used in the research, the data of 16 public and private American institutions of the top-funded American's National Institutes of Health has been investigated (3). In that work, rats and mice constituted approximately 99.3% of the animals used in the research during 2017-2018. Based on that proportion, the total number of rats and mice used was estimated at 111.5 million per year (3).

The quality and validity of the data are important for the reliability of any scientific study (4). Although laboratory animals are usually treated in a controlled scientific experimental environment (5); this environment might not be achieved in all studies. In addition, factors such as health status and blood collection methods can also influence the measured parameters (4). Therefore, the determination of normal reference values for biochemical and hematological parameters is crucial. However, the use of non-local reference values could have a negative impact on the validity of the results (6). Animal breeders usually provide these values upon purchase; yet this service is almost lacking in Iraq. Such a service offers an opportunity to the researchers to validate the estimated parameters, particularly for those of the normal group (2).

In our attempt to collect the normal biochemical values data of laboratory animals in Iraq, we revealed a great inconsistency in the available data, which could confuse the researchers. For instance, from three different studies representing 7 normal male rats, the concentration of aspartate aminotransferase (AST) in each study was estimated at 80.74 U/L (7), 37.8 U/L (8), and 47.28 U/L (9). Similar situation was observed in AST levels in mice, from three different studies representing 10 normal male mice, the AST concentration was reported at 20.03 U/L (10), 285.19 U/L (11), 60 U/L (12). In rabbits, three studies representing 5 to 6 normal male rabbits estimated the AST concentration at 13.5 U/L (13), 35 U/L (14), and 90.8 U/L (15). To our knowledge, normal values of biochemical parameters in laboratory animals in Iraq estimated via meta-analysis are unavailable. Meta-analysis provides robust estimates pooled from a large sample size represented from different studies (16). Therefore, the objective of the current study was to provide normal values of biochemical parameters in laboratory animals pooled from existing studies performed in Iraqi universities using meta-analysis approach. In this analysis, laboratory animals are referred to as rats, mice, and rabbits.

MATERIALS AND METHODS

Ethical Approval

The current study was exempt from ethical approval prerequisites because it was based on the analysis of data only, which were provided from previously published studies.

Data Collection and Preparation

The current analysis was performed according to PRISMA 2020 statement (17); however, an assessment of the retrieved studies was not conducted because it was not an objective of interest. To achieve our objective, we included studies reported original data, used at least one of the laboratory animals of interest (i.e., rat, mice, and/or rabbit), included control groups represented normal animals, published in peer-reviewed journals, and written in Arabic or English. Data were collected and prepared for analysis throughout three consecutive steps by two authors as the following: (i) search strategy (by AA); a step where eligible studies for inclusion were identified, (ii) data extraction (by AA), a step where items required for analysis from the identified studies were collected, and (iii) analytical approach (by MD); a step where that the final list of studies included in the analysis were determined.

Search Strategy

Pertinent peer-reviewed published reports were retrieved from the Iraqi Academic Scientific Journals database, IASJ (https://www.iasj.net/), a database provided by the Iraqi Ministry of Higher Education and Scientific Research that enables searching by journal, subject, or institution. As of August 2024, this database includes 426 open-access peer-reviewed journals from 114 Iraqi institutions. The search was conducted in June 2021 and updated in April 2022. To conduct the search, the words: “rats, mice, rabbit, and biochemical” have been identified by two authors (AA and NM) as keywords that can retrieve as much as possible pertinent studies. Additional words such as biochemistry, clinical biochemistry, Iraq, and lab animals did not add value to the retrieved records. The keywords for rats, mice, and rabbit were entered separately, whereas the word biochemical was added in each round. The keywords were entered in the search box separated by a comma and one space after each word as follows: (i) rats, biochemical; (ii) mice, biochemical; and (iii) rabbit, biochemical. Although the comma did not change the retrieved records number, it was added to facilitate reviewing the keywords. The operators “and” and “or” as Boolean operators between the selected keywords were removed because they did not add value to the retrieved records. In this step, duplicated records were identified and manually removed.

Data extraction

Data were extracted from the retrieved studies and compiled into a Microsoft Excel file (Microsoft Corp. 2010, Redmond, WA). Extracted items included: author(s), year of publication, type of animal used in the study, total number of animals, number of animals in the control group (which represented normal animals), sex, age (months), body weight (g), estimated parameters, unit of estimation, standard deviation/error. Subsequently, data for each animal species were moved to a separate Excel sheet in the same file. In addition, when the retrieved studies used different units of estimation for the same parameter, the units were unified. In this step, the exclusion criteria included: studies did not determine the animals’ sex, studies reported the values of the parameter without sex’s discrimination, studies missed the normal group or did not report the number of animals for that group studies used plasma instead of serum in the analysis, studies examined only pregnant or weanling animals, and studies missed the estimation unit or reported incorrect one.

Analytical approach

In this step, the extracted data were prepared for analysis. Any study that did not report or reported a standard deviation/error value greater than the mean value for a specific parameter was excluded from the analysis of that parameter. Furthermore, when a standard deviation was reported, the standard error was calculated using the reported standard deviation and the number of animals in the control group according to the following equation: (standard error = standard deviation / √ number of animals) (18). The influential observations, i.e., extreme high or low values, that can affect the estimated values, were identified and excluded. In brief, the 1.5 interquartile range (IQR) rule was used to identify those values above the 3rd quartile and those below the 1st quartile using the following equations: [3rd Q + (1.5 × IQR)] and [1st Q – (1.5 × IQR)], respectively. For this purpose, the command "extremes" with the option "iqr" was used in STATA 13.0 (StataCorp., College Stations, TX). Subsequently, records of the identified extreme values were manually removed from the Excel file before the analysis. Finally, we reported the estimate for each parameter only when at least three studies were available for the calculation. We did not report the pooled estimate included a negative 95% CI value because the concentration of the estimated parameters cannot logically be negative. A negative 95% CI value might indicate significant heterogeneity among the values reported by the studies included in the analysis.

Meta-analysis Procedure

In this analysis, random-effects inverse-variance model with DerSimonian-Laird estimate of tau2 was used to obtain pooled means. The use of this model was on the basis of an assumption that true variation in the means among retrieved studies existed due to including different sexes, ages, sites of work, and housing conditions (19). Heterogeneity measures (i.e., Cochran's Q test and I2) were calculated from the data with confidence intervals on the basis of Gamma distribution for Q; random effects (20). Furthermore, potential evidence of bias due to the effect of small study was examined by Egger test; a regression-based test for continuous data (21). Finally, the modeling process was performed using STATA 13.0 (StataCrop., College Station, TX, USA) applying "metan" command with "random" option to perform the random-effects model, and "metabias" command with "egger" option for Egger regression.

RESULTS

A total of 460 records were identified in IASJ, including 260 for rats, 140 for mice, and 60 for rabbits. The final selection processes produced 264 records eligible for statistical analysis, including 171 for rats, 62 for mice, and 31 for rabbits (Figure 1).

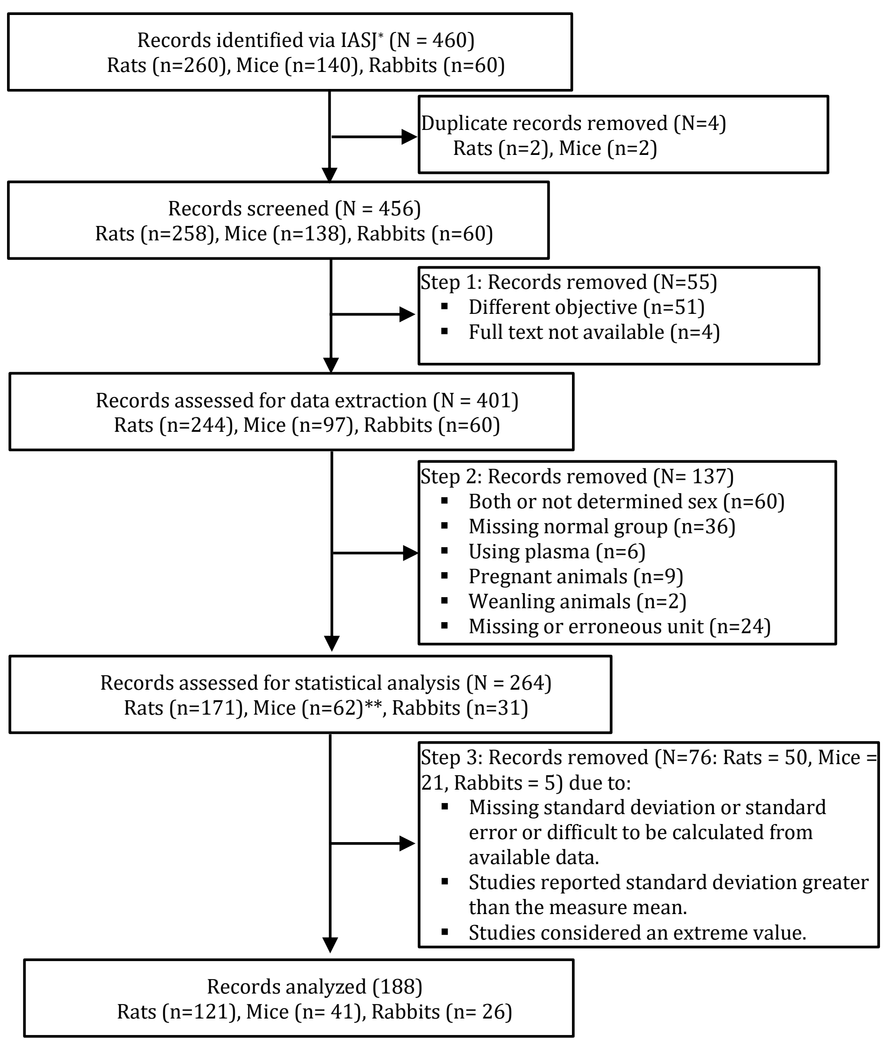

Figure 1. Flow diagram of the process applied to select studies included in the meta-analysis of biochemical parameters in laboratory animals in Iraq

A total of 102 biochemical compounds were reported in these studies, including 85 parameters in rats, 54 in mice, and 54 in rabbits. However, we were able to include only 121, 41, and 26 studies in the analysis for rats, mice, and rabbits, respectively (Figure 1). The distribution of the sample size used in the studies entered the analysis was summarized in Table 1. In addition, the mean ± standard deviation of the ages (months) used in the analyzed studies was 2.8 ± 1.0, 3.14 ± 1.15, and 9.2 ± 3.3 for rats, mice, and rabbits, respectively.

Table 1. Distribution of the sample size of rats, mice, and rabbits used in the studies included in the current random-effects meta-analysis models

	Sample size distribution					
Animal	**Mean**	**Median**	**Minimum**	**Maximum**	**1st quartile**	**3rd quartile**
Rats	8	6	4	36	5	8
Mice	8	8	3	16	6	10
Rabbits	6	6	4	10	5	6

Biochemical Parameters in Rats

The values of a total of 31 biochemical parameters were pooled from 121 studies. A total of 970 rats were used, including 764 males and 206 females, with a sample size ranged between 20 to 460 rats per parameter. Among the 31 parameters, 27 were reported regardless of sex (i.e., overall value), 23 for males only, and 21 for females only. The proportion of variance in the estimated parameters due to heterogeneity was 87.4% - 100%. Finally, evidence of bias due to small studies was found in 10 parameters among 31 (Table 2).

Biochemical Parameters in Mice

The values of a total of 13 biochemical parameters were pooled from 41 studies. A total of 320 mice were used, including 288 males and 32 females, with a sample size ranged between 36 to 144 mice per parameter. Among the 13 parameters, 11 were reported regardless of sex (i.e., overall value), 13 for males only, and zero for females only. The proportion of variance in the estimated parameters due to heterogeneity was 99.5% - 100%. Finally, evidence of bias due to small studies was found in only 2 parameters among 13 (Table 3).

Table 2. Biochemical normal values in rats in Iraq pooled from a total of 121 studies using meta-analysis random-effects models

				Estimate (95% confidence interval)			Overall	Egger's
Parameter	**Unit**	**Studies**	**Size**	**Overall**	**Male**	**Female**	**I^2**	***P*-value**
Enzymes								
Aspartate aminotransferase	U/L	56	430	55.4 (50.5, 60.3)	54.1 (48.8, 59.4)	63.3 (51.1, 75.4)	100%	0.15
Alanine aminotransferase	U/L	58	460	32.0 (28.3, 35.8)	30.5 (26.5, 34.6)	40.4 (25.9, 54.9)	100%	< 0.01
Alkaline phosphatase	U/L	35	261	82.4 (66.4, 98.4)	81.0 (66.2, 95.8)	86.6 (67.4, 106)	100%	0.03
Proteins								
Total Protein	g/dl	22	152	7.5 (6.7, 8.4)	7.4 (6.5, 8.2)	8.2 (6.7, 9.6)	99.5%	< 0.01
Albumin	g/dl	11	79	3.8 (3.4, 4.2)	3.6 (3.4, 3.9)	4.1 (3.1, 5.1)	99.7%	0.44
Globulin	g/dl	5	31	2.6 (1.8, 3.4)	2.5 (1.8, 3.3)	*	99.5%	< 0.01
Hormones								
Progesterone	ng/mL	4	34	-	**	7.2 (6.8, 7.7)	91.2%	0.47
Estrogen	pg/mL	6	47	42.7 (25.9, 59.6)	*	46.5 (21.1, 71.9)	99.6%	0.05
Triiodothyronine	ng/mL	7	56	1.0 (0.83, 1.1)	1.4 (0.81, 2.0)	0.85 (0.81, 0.89)	95.2%	0.21
Thyroxine	µg/dl	7	56	4.6 (3.4, 5.7)	4.1 (2.3, 5.8)	4.9 (4.3, 5.6)	87.4%	0.09
Thyroid stimulating hormone	µlu/mL	3	20	1.0 (0.50, 1.4)	*	*	95.7%	0.64
Follicle stimulating hormone	mlu/mL	5	47	3.0 (2.3, 3.7)	*	4.4 (1.7, 7.2)	99.1%	0.08
Luteinizing hormone	mlu/mL	5	47	5.6 (3.8, 7.4)	*	7.4 (2.9, 11.9)	99.5%	0.15
Testosterone	ng/mL	3	31	-	3.2 (1.1, 5.2)	**	100%	0.63
Minerals								
Calcium	mg/dl	6	37	9.4 (8.8, 10.1)	*	9.8 (9.2, 10.5)	98.4%	0.36
Magnesium	mg/dl	3	20	2.1 (2.0, 2.2)	*	*	98.1%	0.92
Phosphorus	mg/dl	4	27	5.5 (4.9, 6.0)	*	5.6 (4.7, 6.5)	90.9%	< 0.01
Miscellaneous								
Blood Urea Nitrogen	mg/dl	4	25	-	28.1 (16.1, 32.1)	**	99.4%	0.03
Total Bilirubin	mg/dl	10	76	0.46 (37, 0.54)	0.51 (0.39, 0.62)	*	98.8%	0.08
Creatinine	mg/dl	25	190	0.75 (0.53, 0.97)	0.70 (0.47, 0.92)	1.0 (0.0, 2.1)	99.9%	0.76
Urea	mg/dl	35	257	30.4 (26.3, 34.5)	30.3 (16.9, 43.8)	30.4 (16.9, 43.8)	99.9%	< 0.01
Uric Acid	mg/dl	4	30	-	1.5 (1.2, 1.8)	**	96.9%	0.43
Glucose	mg/dl	36	296	96.8 (93.1, 101)	97.0 (92.3, 102)	96.4 (86.1, 107)	99.8%	0.90
Total Cholesterol	mg/dl	55	216	88.1 (73.6, 103)	90.5 (76.7, 104)	73.6 (37.2, 110)	100%	0.54
Triglyceride	mg/dl	47	374	75.1 (65.6, 84.6)	74.7 (64.6, 84.7)	78.9 (24.7, 133)	100%	0.68
High density lipoprotein-cholesterol	mg/dl	33	232	35.0 (26.0, 44.1)	34.6 (25.0, 44.1)	39.9 (7.0, 72.8)	100%	0.34
Low density lipoprotein-cholesterol	mg/dl	30	234	34.1 (26.9, 41.4)	34.8 (26.6, 43.0)	28.6 (7.7, 49.5)	100%	0.46
Very low density lipoprotein	mg/dl	21	144	16.7 (13.9, 19.6)	16.6 (13.7, 19.5)	*	100%	0.47
Phospholipids	mg/dl	4	44	87.2 (79.6, 94.7)	80.5 (78.9, 82.0)	*	94.2%	< 0.01
Glutathione	µmol/ L	13	84	9.8 (7.4, 12.2)	9.5 (8.2, 10.8)	9.4 (0.55, 18.4)	100%	0.23
Malondialdehyde	µmol/ L	13	84	1.9 (1.5, 2.3)	1.9 (1.5, 2.4)	*	99.7%	0.04

* Excluded due to < 3 studies entered the analysis. ** No study available. Study= number of studies included in the analysis, Size=sample size for each parameter

Table 3. Biochemical normal values in mice in Iraq pooled from a total of 41 studies using meta-analysis random-effects models

Parameter	Unit	Studies	Size	Estimate (95% confidence interval)			Overall	Egger's
				Overall	Male	Female	I^2	*P*-value
Enzymes								
Aspartate aminotransferase	U/L	14	139	84.9 (74.2, 95.6)	94.1 (54.7, 134)	*	99.9%	0.10
Alanine aminotransferase	U/L	15	132	32.9 (23.1, 42.7)	32.5 (24.4, 40.6)	*	99.9%	0.67
Alkaline phosphatase	U/mL	10	94	44.5 (24.2, 64.9)	40.1 (26.7, 53.6)	*	99.9%	0.84
Proteins								
Total Protein	g/dl	12	97	5.7 (4.9, (6.5)	5.7 (4.8, 6.5)	*	99.8%	0.13
Albumin	g/dl	5	37	-	3.5 (2.8, 4.1)	**	99.9%	0.48
Miscellaneous								
Urea	mg/dl	12	107	31.3 (27.2, 35.4)	31.6 (27.0, 36.2)	*	99.5%	0.06
Creatinine	mg/dl	12	103	0.55 (0.36, 0.73)	0.55 (0.34, 0.76)	*	99.5%	0.72
Bilirubin	mg/dl	4	36	-	0.45 (0.15, 0.75)	**	100%	0.26
Glucose	mg/dl	15	105	124 (99.6, 148)	120.3 (90.0, 151)	*	100%	0.30
Total cholesterol	mg/dl	19	144	144.1 (128, 160)	142.2 (125, 159)	*	99.9%	0.07
High density lipoprotein-cholesterol	mg/dl	9	89	59.3 (37.5, 81.0)	62.6 (39.5, 85.6)	*	100%	0.69
Low density lipoprotein-cholesterol	mg/dl	6	60	53.6 (34.6, 72.7)	48.5 (27.7, 69.3)	*	99.9%	0.94
Triglyceride	mg/dl	11	81	124.1 (92.4, 156)	126.4 (93.1, 160)	*	100%	< 0.01

* Excluded due to < 3 studies entered the analysis. ** No study available. Study= number of studies included in the analysis, Size=sample size for each parameter

Table 4. Biochemical normal values in rabbits in Iraq pooled from a total of 26 studies using meta-analysis random-effects models

Parameter	Unit	Studies	Size	Estimate (95% confidence interval)			Overall	Egger's
				Overall	Male	Female	I^2	*P*-value
Enzymes								
Aspartate aminotransferase	U/L	15	90	38.6 (23.2, 54.0)	38.4 (24.1, 52.8)	39.2 (18.4, 56.0)	100%	0.01
Alanine aminotransferase	U/L	15	90	31.7 (24.5, 38.8)	33.1 (26.2, 39.9)	28.2 (11.2, 45.3)	99.9%	0.23
Alkaline phosphatase	U/L	7	48	41.2 (32.0, 50.3)	46.3 (28.9, 63.7)	*	99.9%	0.03
Proteins								
Total Protein	g/dl	9	58	6.6 (5.7, 7.5)	6.7 (5.4, 7.9)	6.5 (4.9, 8.1)	98.5%	0.13
Albumin	g/dl	6	36	3.1 (2.6, 3.5)	2.9 (2.3, 3.4)	*	68.2%	0.69
Globulin	g/dl	3	26	2.5 (1.5, 3.6)	*	*	95.7%	0.52
Miscellaneous								
Glucose	mg/dl	10	68	106.5 (97.4, 115.6)	97.5 (92.6, 102.4)	124.3 (102.8, 146)	98.6%	0.20
Urea	mg/dl	6	38	-	46.9 (20.7, 73.1)	**	100%	0.70
Creatinine	mg/dl	8	49	1.0 (0.83, 1.2)	1.1 (0.81, 1.3)	*	98.7%	0.16
Triglyceride	mg/dl	7	48	88.9 (73.4, 104.4)	92.1 (75.5, 108.7)	*	99.6%	0.66
Total cholesterol	mg/dl	10	69	103.1 (94.0, 112.2)	98.7 (86.5, 110.9)	112.9 (90.8, 135.0)	99.1%	0.26
High density lipoprotein-cholesterol	mg/dl	4	27	28.5 (12.8, 44.1)	*	*	100%	0.40
Low density lipoprotein-cholesterol	mg/dl	5	37	53.1 (33.4, 72.8)	55.9 (22.0, 89.9)	*	99.5%	0.36
Very low density lipoprotein	mg/dl	4	32	19.6 (13.1, 26.0)	21.6 (15.7, 27.5)	*	99.3%	0.07
Malondialdehyde	μmol/L	4	22	1.6 (1.4, 1.8)	***	*	99.8%	0.26

*Excluded due to < 3 studies entered the analysis. ** No study available. *** Not reported; 95% CI included a negative value. Studies= number of studies included in the analysis, Size=sample size for each parameter

Biochemical Parameters in Rabbits

The values of a total of 15 biochemical parameters were pooled from 26 studies. A total of 164 rabbits were used, including 120 males and 44 females, with a sample size ranged between 22 to 90 rabbits per parameter. Among the 15 parameters, 14 were reported regardless of the sex (i.e., overall value), 12 for males only, and 5 for females only. The proportion of variance in the estimated parameters due to heterogeneity was 68.2% - 100%. Finally, evidence of bias due to small studies was found in only 2 parameters among 26 (Table 4).

DISCUSSION

Our objective of the current project was to provide robust normal values for as many as possible biochemical parameters in laboratory animals in Iraq. Combination of the reported values via meta-analysis approach can overcome the controversies arising from different studies and provide the researchers references from local studies that can help validate their estimations. We were able to pool 31 biochemical parameters in rats, 13 in mice, and 15 in rabbits. An additional advantage of our analysis conducted here is identifying potential pitfalls in reporting the data in previous studies that can be overcome in future studies.

Biochemical Parameters in Rats

We observed differences in the estimated values between male and female rats, although we were unable to report values for both males and females of some parameters due to either unavailable or few available studies for analysis. The differences in the estimated values between males and females reported here are in line with previous studies such as those for Delwatta et al. (2) and He et al. (22), regardless of which parameter is higher in males or females. Sex-specific differences in the biochemical parameters' values are attributed in the literatures to the difference in physiology between both sexes. Some of the parameters values we reported in the current analysis are in line with previous studies. For instance, the concentration of AST reported in the current study was

55.4 (50.5, 60.3) U/L for combined sex, 54.1 (48.8, 59.4) U/L for male and 63.3 (51.1, 75.4) for females, which is considered within the ranges of the values reported by He et al. (22) for Sprague-Dawley rats (59-139 U/L, combined sexes) and Wistar rats (50-96 U/L for male, and 61-153 U/L for female). However, several factors can play a role in the variability of the estimated values such as feeding (23), as well as the techniques and reagents used in the measurement (22). In addition, age of the animals has an important impact on the estimated values, although the mean of age of rats in our analysis was 2.8 ± 1.0 months, which is comparable to the approximately 9 weeks old used by He et al. study (22). Moreover, differences in the breed could have an additional role in the differences in the values estimated in this study compared to other studies; however, it is difficult to indicate the breed in this study because most breeds used locally are mixed breeds.

Some of the pooled values in our analysis had wide confidence intervals. For instance, the mean of HDL-C being female was estimated at 39.9 mg/dl with 95%CI 7.0 to 72.8, which reflects the differences among the values reported in the retrieved studies as a result of factors that might alter the measurements such as the feeding and measurement methods (22, 23). In addition, the proportion of variance in the estimated parameters due to heterogeneity was large (87.4% - 100%), which indicates a true variation in the estimated values reported in the local literatures. This magnitude of heterogeneity was expected; therefore, we performed the random-effects model to pool the values.

Biochemical Parameters in Mice

In this analysis, we provided the values of laboratory parameters in male mice only due to the few studies were available for the analysis in female mice. Therefore, we were unable to indicate sex-specific differences in the estimated values in mice. Though, previous studies reported differences in the values in mice between males and female, such as Otto et al. (24), Barbosa et al. (25), and Smith et al. (26). The values provided in our analysis are in line with values reported by other authors worldwide. For example, the mean of total protein concentration in males in our analysis was estimated at 5.7 g/dl (95% CI 4.8, 6.5) compared to 4.9 g/dl (4.4, 5.8) reported by Smith et al. (26) and 49.8 g/L (47.5, 52.0) reported by Otto et al. (24) as well as values reported by Boehm et al. (23). However, differences in some values between our and other reports were observed. For instance, we estimated the GPT concentration at 32.9 U/L (95% CI 23.1, 42.7), which is considered slightly higher than that reported by Smith et al. (26) at 18 U/L (12-34), and lower than that of Otto et al. (24). As that for rats, the differences could be attributed to the differences in the experimental conditions, feeding methods, and techniques used in the measurement, as well as differences in the age and breed of mice used in the retrieved studies in our analysis compared to other studies around the world. Nevertheless, it is difficult to indicate the breed in this study because most breeds used locally are mixed breeds. All these differences could explain the magnitude of the heterogeneity observed in meta-analyses performed in the current study, which was considered high (i.e., 99.5-100%). Thus, to avoid erroneous pooled values, we performed random-effects model in our meta-analyses.

Biochemical Parameters in Rabbits

We observed differences in the estimated values between male and female rabbits, although we were unable to report values for both male and females of some parameters due to the few available studies for the analysis. The sex difference was minor except that for glucose (i.e., 97.5 mg/dl (95% CI 92.6, 102.4) in males, compared to 124.3 mg/dl (95% CI 102.8, 145.8) in females) and total cholesterol (i.e., 98.7 mg/dl (95% CI 86.5, 110.9) in males, compared to 112.9 mg/dl (95% CI 90.8, 135.0) in females). One reason might be the function of these differences is the techniques and reagents used in the analysis among the retrieved studies. Another reason is a function of sex-related physiology such as energy demand and sensitivity to insulin in males compared to females (22). Nevertheless, the values reported in the current analysis are generally in line with those reported by Shousha et al. (27) and Özkan and Pekkaya (28). The minor differences between our analysis and other studies could be attributed to the differences in housing, feeding, and techniques used in the measurement, as well as the age and breed of rabbits used in the studies. For instance, the rabbits used in the retrieved studies in the current analysis were 9.2 ± 3.3 months old, which were close to the ages used by Shousha et al. (27); i.e., 8-12 months. These minor differences could explain the least heterogeneity observed in meta-analyses for rabbits compared to rats and mice (i.e., 68.2% - 100%), although we performed random-effects model in our meta-analyses.

Although meta-analysis provides robust estimates pooled from the large sample sizes represented from different studies (16), our analyses here had some limitations. First, some parameters were estimated for only males or females because of the limited number of studies eligible for these current meta-analyses. Second, evidence of heterogeneity was high, reflecting the variability among values reported by the retrieved studies; however, it was overcome through implementing the random-effects model. Finally, evidence of bias due to the small study effects was evident in some studies, nevertheless; the majority of the values reported here were in line with the values reported worldwide.

Our current analysis provides values for different biochemical parameters in rats, mice, and rabbits that can help researchers verify their measurements or use these values as reference values. We encourage researchers to consider the values we provided in this analysis. In addition, we ought the researchers to report the details of the sample size, number of animals in each group, sex, exact age, and the accurate units for the estimated values in their studies to facilitate further analyses for more reference values in future analyses.

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N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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القيم الكيموحيوية للحيوانات المختبرية في العراق: دراسة تحليل ميتا

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الخلاصة

كان الهدف من الدراسة هو تقدير القيم الطبيعية للمعايير الكيموحيوية للحيوانات المختبرية في العراق. تم تجميع القيم من الدراسات التي أجريت في الجامعات العراقية وذلك باعتماد التحليل التلوي. تم استرجاع الدراسات المنشورة من قاعدة بيانات المجلات الأكاديمية العلمية العراقية. تم اعتماد نموذج التباين العكسي للآثار العشوائية للحصول على معدلات القيم الكيموحيوية من الدراسات المؤهلة للتحليل، فمن أصل ٤٦٠ عنواناً تم تمييز ٢٦٤ بحثاً مؤهلاً للتحليل الإحصائي شملوا على ١٠٢ معيار كيموحيوي. بلغ معدل حجم العينة المستخدمة في الدراسات ٨ للجرذان، و ٨ للفئران، و ٦ للأرانب. بلغ معدل الأعمار (± الانحراف المعياري) ٢,٨ شهراً (± ١) في الجرذان، و ٣,١٤ شهراً للفئران (± ١,١٥) و ٩,٢ شهراً (± ٣,٣) للأرانب. تم قياس ٣١ قيمة في الجرذان من أصل ١٢١ دراسة، و ١٤ قيمة في الفئران من أصل ٤١ دراسة، و ١٥ قيمة في الفئران من أصل ٢٦ دراسة. ميّزت دراستنا نسبة تباين كبيرة بسبب عدم التجانس في المعدلات التي سجّلتها الدراسات. خلال دراستنا، نحث الباحثين على اعتماد القيم التي قدمناها في ضوء هذا التحليل، كما نحثّهم على بيان تفاصيل حجم العينة وعدد الدراسات في كل مجموعة فضلاً عن بيان أجناس وأعمار الحيوانات المستخدمة في دراساتهم من أجل إتاحة الفرصة لتقدير المزيد من القيم في تحاليل تلوية لاحقة.

الكلمات المفتاحية: قيم طبيعية، جرذ، فأر، أرنب، تحليل ميتا