

REVIEW

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# Global trend of clinical biomarkers of health and disease during the period (1913–2021): systematic review and bibliometric analysis

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## Abstract

**Background:** The literature review provides a concise and detailed description of the available and published data on the investigated research problem. The study summarizes findings over the last 100 years regarding clinical biomarkers during health and disease. Research expanded to present the range of enzyme acetylcholinesterase in human blood utilizing diverse methodology during the 1949–2021 year.

**Main body:** Data analysis includes program SPSS v23.0, frequency, percentage, numbers and graphical presentation of results. Information from the papers gathers in Microsoft Excel 2007 and contains information: study type, journal, publisher, year of publication, continent, the health status of respondents, biomarkers, number and age of participants, types of samples, methodology, goals and conclusions. Data collection includes electronic databases, the National Center for Biotechnology Information and Google Scholar, with several inclusion criteria: (1) anthropometry (2) urine (3) blood in the healthy and diseased population parameters during different physiological states of the organism. The initial number of collected and analyzed papers is 1900. The final analysis included 982 studies out of 1454 selected papers. After the selection process, 67.53% remains useful. The range of enzyme acetylcholinesterase included 107 publications.

**Conclusion:** The number of published scientific papers has been increasing over the years. Little practical information in scientific and clinical practice exists. There is an urgent need for concise highlighting of literature key arguments and ideas. Results apply to a specialized area of research.

**Keywords:** Systematization of literature, Human biomarkers, Health, Disease, Physiology, Enzyme acetylcholinesterase

## 1 Background

A boosting number of scientific publications are available on the market. Efficacious information transition to the public lacks, and it is becoming time-consuming to find all the appropriate facts. The vast expanse of academic papers retains in place by swirling quantitative and qualitative data currents. This drifting publication growth rate stretches from about more than a million published articles per year across all continents [1]. The original

idea was to share knowledge [2]. The problem is that it is not quite like that [2]. It is almost like the availability of data discrepancy of the content exists [2]. It is hard to find appropriate information in the sea full of data. It is an endless chase for diverse scientific fields, so questions are appointed. How to choose the best relevant data for your research? What kind of information professionals want to obtain, and why? Accumulation data without functional applicability over time are more than evident [2, 3]. Information discrepancies can be ease by the selection and presentation of good quality research. Develop ideas by expanding the meaning of the research question. Determine the strengths, weaknesses, opportunities and

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threats for sample material, finance, time for writing and quality of published information. A positive or negative outcome can arise from eternal or external factors. Competitiveness for writing articles rose and can have a negative impact on science [2, 4].

It is significant to identify influencing factors, research design, management training and links to industry/commercial stakeholders for funding successes [5]. Research collaboration, environmental assessment and improving research competence help alleviate effective scientific communication [5]. Good quality science requires a convincing story, an appropriate way of presenting data, discussion and conclusion remarks [6]. The collection of quality data and thinking in the right direction is significant for article publishing. Pressures of publishing scientific information in journals are enormous [2]. New knowledge is less created [2]. Market demands influence the quality of published data [2]. Science should be discovering new, undiscovered pathways by presenting high impact information in international journals [7]. Results have a positive impact on society regarding sustainability, applicability, usage and publicity [7]. These project activities lead to the accumulation of new knowledge recourses and future activities [7]. Published and proven information summarizes the ideas to the broad scientific community. This study review summarizes extensive systematic literature that can apply in urine system oncology, genitourinary medicine and reconstructive urology. Reduce un-useful data by raising awareness for publication directions and achievements involving broad anthropology, blood and urine biomarkers. The study also focuses on the reference range of the enzyme acetylcholinesterase (AChE), a biological molecule with a wide distribution and application. Cholinesterases are neurotransmitters that catalyze the hydrolysis of the cholinergic neurotransmitter acetylcholine [8]. Based on substrate and inhibitor specificity, cholinesterases classify as AChE and butyrylcholinesterase (BChE). [8]. The catalytic role of the enzyme AChE reflects the synaptic and nonsynaptic hydrolysis of acetylcholine (ACh). The noncatalytic function of the AChE enzyme reflects brain development, regeneration and neuronal modulation [9]. AChE is involved in cell adhesion, cell recognition, morphogenesis, differentiation, cell proliferation and angiogenesis. It promotes hematopoietic growth and increases during physiological stress and head injury [9]. It is a potential marker of apoptosis, oxidative stress and tumor suppressor [9]. The enzyme AChE activates JNK, MAPK/PI3K, Apaf1, Cit C, Caspase 9, WNT/ $\beta$  catenin signaling pathway [10, 11]. Plasma cholinesterase activity is a potential biomarker for postoperative delirium after noncardiac surgery in the elderly [12]. The association between the

enzyme AChE and apoptosis representing a new ethanol mechanism that leads to brain cell damage has been identified [13]. AChE activity is associated with symptoms of depression and anxiety in adolescents reflected near pesticide-sprayed sites [14]. The AChE gene is expressed in sperm and participates in cell apoptosis [15]. The enzyme AChE is a potential target for chemical and biological bioterrorism because it is associated with war toxins such as aflatoxin B1, sarin and pralidoxime [16, 17].

The hypothesis postulates that research publications contain un-useful information among other publication. The objective of the paper tackles defined research output. Clearly describes published information input, justification, study capacity and excellence, utilization of resources and shows the excellent track of the record. The goal was to provide a description, summary and critical evaluation of the literature. Logically develop arguments and ideas. Construct a good quality literature research and improve the ability to communicate fundamental data effectively to the public. Research results influence acquiring new functional knowledge and provide peer support.

## 2 Main text

### 2.1 Methods

Literature collection with database NCBI and Google Scholar apply for article search during the 1913–2020 year. Searched terms were parameters of anthropometry, urine and blood biomarker in the healthy and diseased population. The content relevance of published papers influences the data selection process. The total number of selected literature at the beginning of the study was 1900. Fast skimming of the content and paper duplications striking out determined 1454 papers for further analysis. After the data extraction in Microsoft Excel 2007, based on information relevance, studies were excluded. The final selection of articles leads to a total number of 982 papers analyzed in this study. Using standardized data collection form and Microsoft Excel 2007, the following study characteristics were extracted authors last and first name with publication name, publication year, journal and publisher, country and continent, health status, assessed parameters and questioners information, number and age of participants, gender, sample types, methodology, aims, conclusions. In additional 107 papers from the 1949 to 2021 year of publishing, AChE reference range is determined. Publication year, aim, health status, anticoagulants and freezing temperature, participant number, units, sample type, the reference range of AChE and BChE during health and disease, statistical software, experimental method, wavelength, substrate, inhibitor and conclusion as a source of information is determined.

### 2.2 Statistical analysis

Data analysis was performed by IBM SPSS software version 23.0 with percentages (%), counts and graphs presentation.

### 2.3 Results

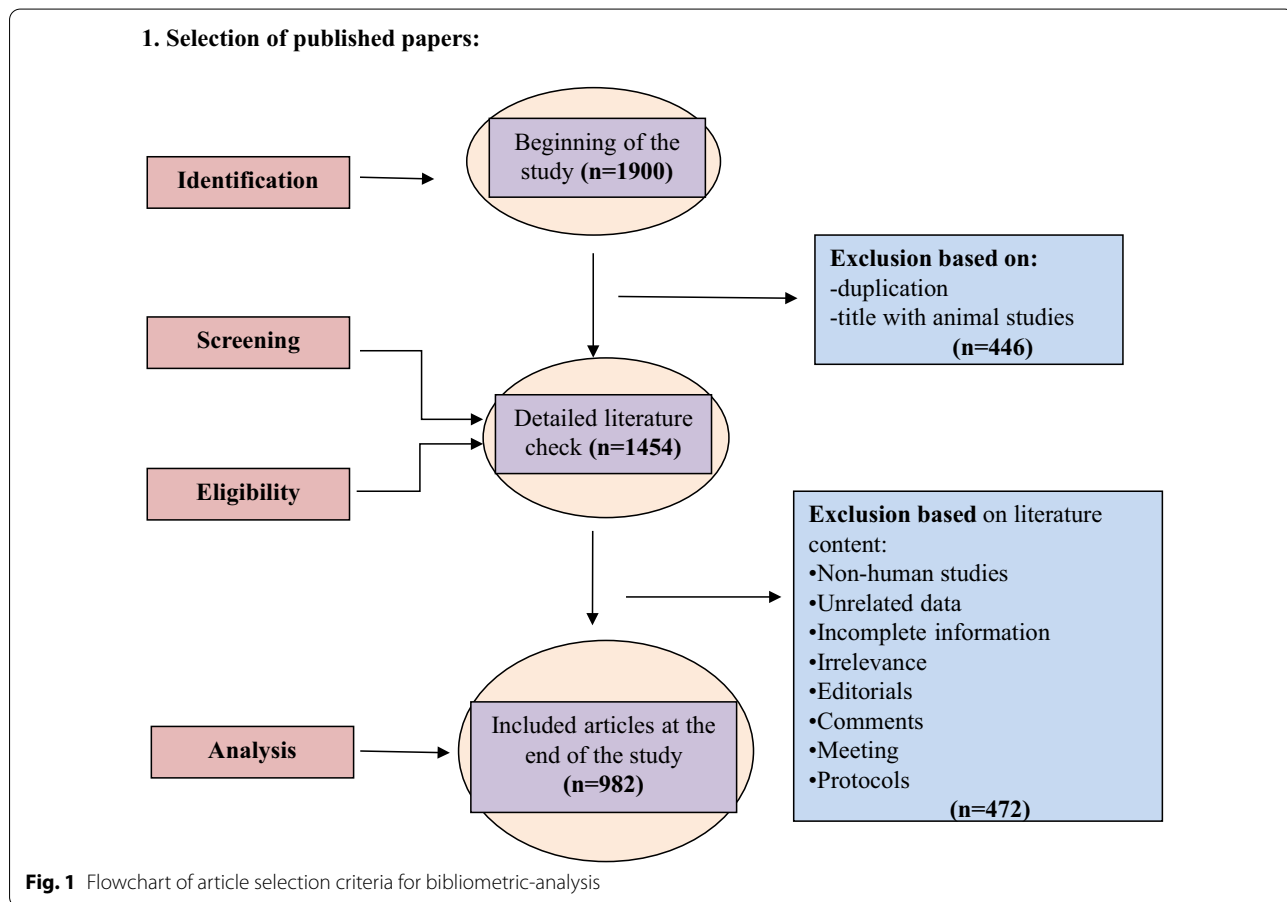
Results are present in VI main areas: (1) study characteristics; (2) sample type and biomarkers; (3) participant information; (4) material and methods; (5) aims and conclusion and (6) reference range of enzyme AChE.

#### 2.3.1 Study characteristics

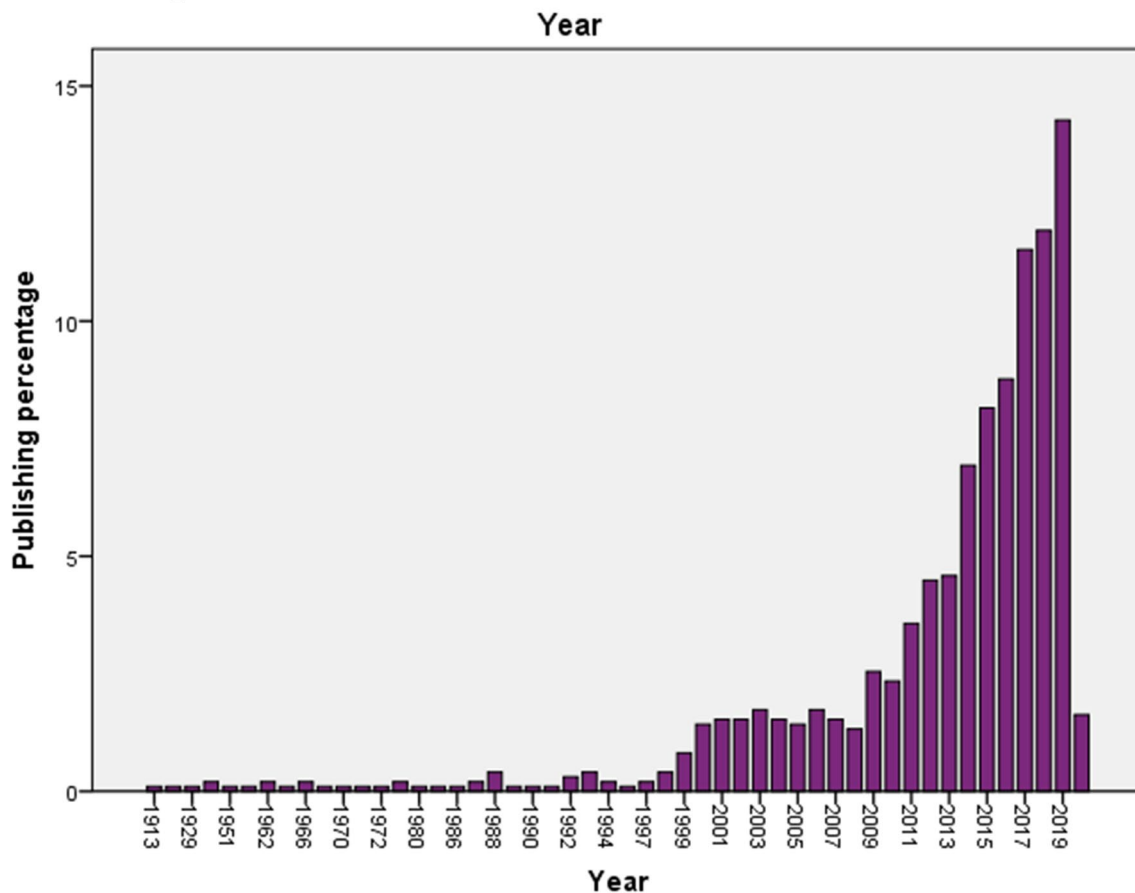
Figure 1 shows information about the paper selection process as a flow chart. The most prevalent number of papers before the intensive selection contains anthropometry parameters (25.58%). The share of the market decreased after the selection process (25.15%). This study shows a 0.43% decrease in quality data after selection. It was noticeable that the market share of blood parameters articles reached a high (8.91%) after the final article selection, with the peaks being lower before the selection process (53.72%) in comparing after the selection process (62.63%). The urine parameter decreased in publications

after the selection process (20.70% to 12.22%). After the selection process, the market share of articles published regarding blood parameters arose from approximately the same level as the urine parameter decreases. However, a minority of totally selected papers (8.18%) contained more than one mentioned investigated sample parameter in the study, other sample parameters or none. In total, 982 publications remain in Microsoft Excel. The selected data summarize in Additional file 1.

The most common publications were in Journals Plos One (5%), Scientific reports (1.4%) and European Journal of Clinical Nutrition (1.4%). The most common publisher is Elsevier, with an incidence of 44.8% (440 publications). The second most common publisher is Springer Nature, with 31.3% (307 publications) incidence. These show a 1.43-fold increase (84 publications) incidence for Elsevier publishers. The market share of Wiley publishers reached a high of 8.6% during this period. Wiley publisher comparing to Elsevier and Springer Nature decreased from about 5.20 to 3.64 fold. Figure 2 summarizes percentages of published papers by year, from 1913 to 2020 year. The most prevalent year of publication is 2019 (140 publications, 14.3%), whose number rose dramatically from



**2. Year of publication:**



**Fig. 2** Percentages of published journals per year during the 1913–2020 year

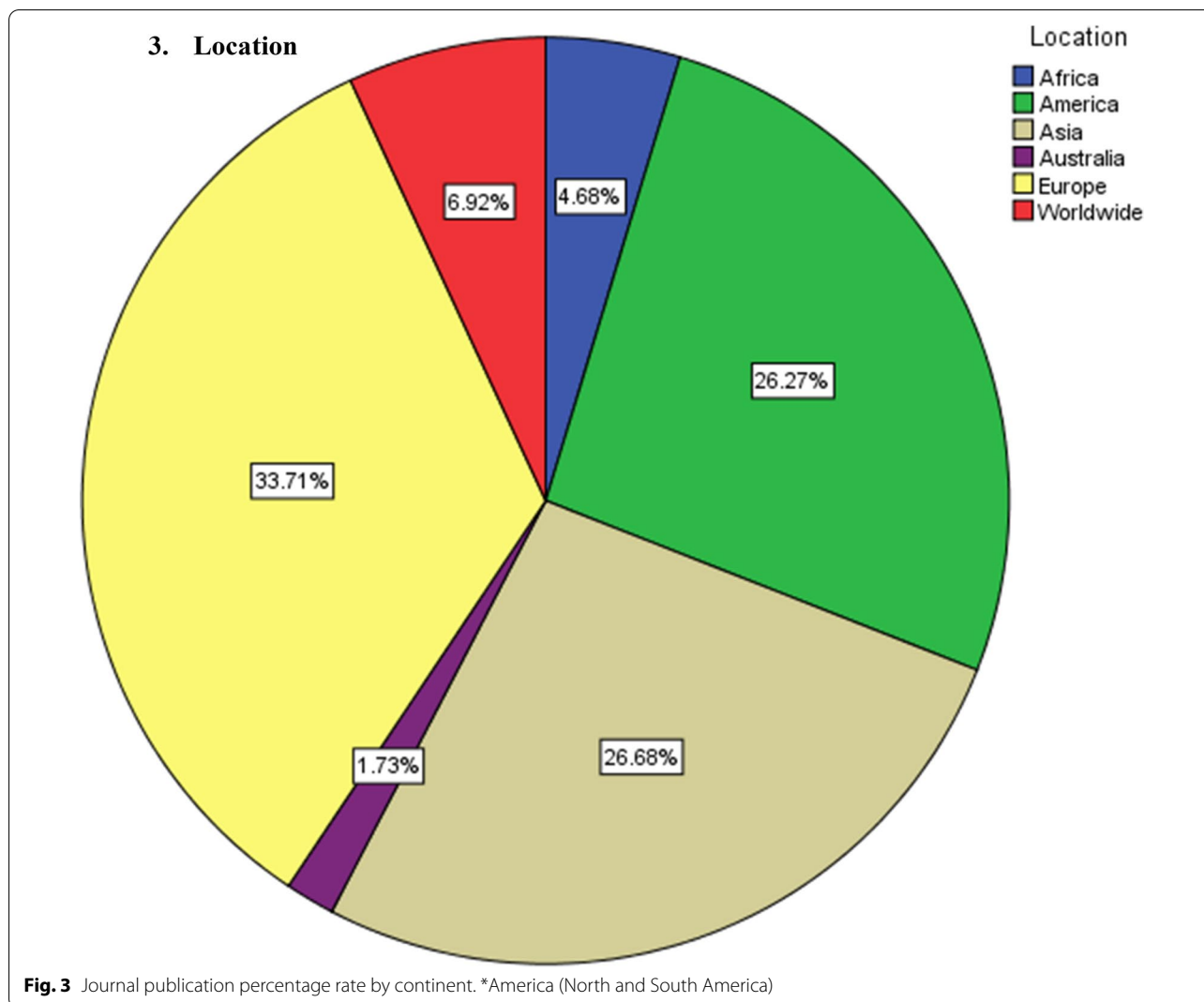
1999 to the 2019 year with a rate of 15.2%. There was a 15-fold increase over the period. The number of published papers hit a percentage-wise low in the 1913 year (0.1%) and remains erratically stable to the 1987 year. It was noticeable that the article publication share started accumulating from the 1988 year, with sudden fall and then leveled off to the 1992 year. The number of publications fluctuated from 1992 to the 1999 year. We have a gradual sharp surge rise from 1999 to 2019 year. It is clear that trend of academic publication increases and is dominant over the years. During the 2014–2017 year, the proportion of publications had a fivefold increase (6.9%, 8.15%, 8.8%, 11.9%) retrospectively. There was a similar publication rate for 2018 and 2017 year (12%). So far, in 2020, we have only a few publications (16; 1.6%).

Published articles fall into several categories: observational, clinical, review, mixed study and not stated. The majority of the study type was observational (41.8%) and not stated (35.5%). The review study type was 15.4% retrospectively. The mixed study type hit the lowest point

with 0.8%. The most common publishing journal for clinical study type was Drug Design and Therapy (0.2%). The abundance of mixed study type falls in the American Journal of Hypertension, Collegium Antropologicum, Environmental Health and Preventive Medicine, International Journal of Advances in Medicine, International Journal of Morphology, Lancet, Plos One (0.1%). Observational study type published in Plos One (2.5%). Review study type accounted highest for the European Journal of Clinical Nutrition (0.5%). The clinical study type is published in Plos One, while the not stated study type is in the American Journal of Hypertension and Plos One journals. Figure 3 shows the changes in the proportions of publishing articles by continent between 1913 and 2020 year, along with the total percentages of publications.

**2.3.2 Sample type and biomarkers**

Published literature became saturated with sample diversity. Providing information from more common samples



like blood, urine, anthropometry to less common as CSF, tissue, cell lines, feces, saliva, sweating, tears, neurofilaments, pleural fluid. Only a few studies have no sample status.

Literature samples include blood, urine, anthropometry, others and not stated. The most common sample type is blood and anthropometry (39.5% and 25.2%). This study shows a 1.56-fold increase for publications with blood samples comparing to anthropometry measures. It is noticeable that other sample types have a prevalence of 20.1%, which is 1.96- and 1.25-fold higher than blood and anthropometry samples. Urine sample utilization (12.2%) hit low for 3.24-, 2.01- and 1.65-fold comparing to blood, anthropometry and other sample types. In published studies, authors usually combined blood samples with anthropometry, CSF, saliva, tissue and urine in total (54.8%) published articles. Urine sample types combine with blood and tissue samples, making a total incidence

of 12.53 percent. This result means that unmixed (without these data) other and not stated sample types in the study have a prevalence of 4.68 and 3.1%. Blood sample type is the most prevalent, with an incidence of 54.58%. This result is 0.72-fold higher in comparison with the first table.

Published articles contained questionnaires with additional information regarding education, occupation, socioeconomic status, income, cognitive data, personality, family history of the disease, genetics, environment, smoking and alcohol consumption, fluid intake (coffee, water, juice), vitamin supplementation, physical activity/inactivity, cough capacity, metabolism. Anthropometry studies included a systematic measurement of the body. The majority (90% out of total number) of published articles contained information regarding: height [thigh clearance, sitting popliteal, knee, knee-heel], weight [body weight loss (BWL%), body weight change

(BWC)], circumference [head, neck, chest, hip, abdomen, wrist, calf, arm (mid arm, mid-arm muscle, mid-upper arm, upper arm)], mass [body mass (BM), body mass index (BMI)]; muscle mass (MM); [skeletal mass muscle (SMM%), appendice index (ASMI), total body (TBSM), total body index (TBSMI)]; lean mass [%], appendice (ALM), appendice index (ALMI), muscle (LMM), lean body mass (LBM), dry lean mass (DLM)], waist [W, hip ratio (WHR), height ratio (WHtR), stature ratio (WSR)], fat [body (BF), truncal mass (TFM), free mass (FFM), mass index (FMI), free mass index (FFMI); belly; free fat acid (FFA), adiposity, soft tissue mass (STM)], skinfold [triceps thickness, sub-scapular, sub-scapular thickness, biceps, triceps, calf, sub-scapular, supra iliac, bicipital, limb, girth, breadths, abdominal, thigh, medial calf thickness, triceps thickness], thickness [(width, chest diameter, tight muscle, skeleton)], blood pressure [systolic, diastolic], heart rate (HR)]. By contrast, the minority (10% out of total number) of published articles contained information regarding water amount [total fluid intake, total body (TBW), extracellular (ECW), intracellular (ICW), hydration/dehydration status, body temperature], nutrition status [energy intake, protein status, total calories carbohydrate]; individual organ function measurement [lung (left, right), static lung compliance (cst), V<sub>O</sub>max, kidney (glomerular filtration rate, GFR), liver function, vertebra, brain (short-term memory, STM), severe motor impairment (SMI), mental component summary (MCS)], breadth [shoulder, hip breadth, foot, Z score], diameter [wrist, knee, ankle, femur, abdominal sagittal diameter to height (SADH), bifilac biacromin], length [arm, leg, elbow, elbow to elbow, foot, palmar, middle finger, up lift, knee-heel, trunk, finger, limb, femur], width [shoulder, hip, bicondylar and biepicondylar, palm], distance [philtrum, chanthal, palpebral fissure, elbow amplitude], index [C, bone strength index (BSI), foot index (FI), abdominal diameter index (ADI), a body shape index (ABSI), body adiposity index (BAI), appendicular lean soft tissue index (ALSTI), bust to hip ratio (BHR), cubic splines], hand dominance, biceps, triceps, grip strength (hand), area arm muscle (AMA), arm fat (AFA), mid-arm muscle (MAMA), mid-upper arm fat area (AFA), forearm muscle area (FAMA), stature, sitting [height erect, shoulder height (SSH), elbow height, elbow length (SEL), buttock popliteal length anthropometric measure chair (AMC)], metabolic state [load capacity metabolic indices (LCMI), basal metabolic rate (BMR)].

An overwhelming majority of studies with blood parameters include biochemistry parameters (75% out of total number) protein [albumin, globulin]; sugar [glucose]; ions [Na, K, P, Cl, Ca, Mg, HCO<sub>3</sub>, Fe]; and others [blood urea nitrogen (BUN), creatinine, cholesterol, HDL, LDL, bilirubin, uric acid, urate, TSH, ALT, AST,

AMT, CO<sub>2</sub>; adiponectin, leptin; ChE (AChE, BChE)]; hematological parameters following published studies claimed reports regarding WBC, RBC, PLT, NE, LY, MO, EO, BA, Hg, Ht, MCV, MCH, MCHC, MPV and CRP. The tinier part (25% out of the total number) of the articles provided a collection of factual knowledge about diverse blood parameters. Studies included markers like oxidative stress marker, inflammation marker [prostaglandin, VEGF, IL-1, 2, 6, 8, 10, 15; Ig-E, A, G; CD4, CD8; macrophage inflammatory protein (MIP-1Beta), IFN-gama, angiogenin, falistatin, kalikrein, carcinoembrionic antigen (CEA),  $\alpha$ -synuclein (SNCA), serum amyloid P, neuroregulin 1 (NRG-1), retinal binding protein, prolactonine]; ions [selen, zinc, magnesium, cobalt, copper, manganese, molybdenum, aluminum, barium, boron, bromide, cadmium, caesium, iodum, lithium, mercur, molibden, nickel, protactinium, rhenion, silicon]; proteomic, antigen [carcinoembrionic antigen (CEA), tumor Ag; nuclear matrix protein (NMP), MAPK, PK, interaction proteins, fibrinogen, RAS oncogen, adiponectine, ceruloplazmine, finrinogen, alfa-amilase, alcal phosphatase, aquaporine-1, perilipin 2, mioglobulin, cystein-C, insulin; macrophage inflammatory protein-1alpha (MIP-1alpha)]; transcriptomics [RNA markers (m, r, micro)]; metabolomics [carbamide nitrogen, ferritin light chain, ammonia, nitrogen, norepinephrine].

Published journals with urine topics contained details about urine osmolarity and specificity, color, blood, protein (creatinine, albumin), gravity, metabolic rate, uric acid, ammonia, nitrogen, glucose, ions (Na, K, Ca). Additional tumor markers are tissue, saliva and CSF. Biomarker includes information regarding tumor size, TNM stadium, metastasis, health status, oxidative stress marker, APOE E4, chit-1, abeta42, n-tau and ceruloplasmin material. Very few studies (1% out of total number) included additional parameters from sweat and tears.

### 2.3.3 Participant information

Over the past hundred years, there have been a dispersing number of study participants. The minimal number of included study participants was one. By contrast, the maximum number of participants was in the range of million (65,712,029). The age of participants ranged from 0 to 100 years. Papers provide information about the stated health status of participants in the journals. In this study, health status includes health, disease, both and not stated. Group disease contained patients with the disease, ranged from cancer, neurodegeneration (ALS, AD) and others (kidney, lung, colon). By contrast, group healthy contained healthy participants. Group both have the disease and healthy control patients. The group not stated included studies without the health status of participants.



Published articles contain information about disease participants (47.5%, 466 publications), healthy participants (35.4%, 348 publication) and both participants (13.6%, 134). By contrast, fewer articles had not stated participant information, 3.5% (34 out of the total number).

For eleven decades, scientists queued to experience healthy and diseased individuals in publications. Healthy individuals apply as a reference or controlled subjects. In selected published articles, disease patients included a vast number of states: weight loss (fasting, dieticians, famine malnutrition, sarcopenia, cachexia); pituitary gland (metabolic syndrome, growth disorder); eye (glaucoma); teeth (dental problems, caries); lung (tuberculosis pleurisy, para-pneumonic effusion, pulmonary tuberculosis); liver (liver cirrhosis); pancreas (diabetes mellitus, overweight, chronic pancreatitis); gaster (gastrectomy); kidney (albuminuria, kidney stones, hemolytic uremic syndrome, renal disease, acute and chronic kidney disease, nephropathy, renal failure, nephrolithiasis); prostate (prostate hyperplasia, glucosuria); cardiovascular disease (hypertension, tachycardia, cardiometabolic risk, chronic heart failure, myocardial infarction); autoimmune disease (celiac disease, multiple sclerosis, HIV, systemic inflammation, systemic lupus erythematosus, leukemia); infectious and inflammation disease (venereal disease, bacterial infections, porphyromonas gingivalis infection, rheumatoid arthritis, gout, pyelonephritis nephrolithiasis, poliomyelitis, hepatitis B and C, syphilis, infectious mononucleosis, sepsis, ebola, human T lymphocyte virus type 1, periodontitis, malaria infection, thyroid fever, Sjogren syndrome, dengue); changes in blood (phlebotomy, hypovolemia, hyperviscosity, hematology disease, thalassemia, sickle cell disease, thrombotic disease, anemia, thrombocytopenia, leucocytosis, leucopenia, hypoglycemia, hypo/hyper kalemia, hyponatremia); brain (Parkinson disease, Alzheimer disease, amyotrophic lateral sclerosis, myasthenia gravis, cerebral palsy, epilepsy encephalopathy, Sanfilippo syndrome, mild cognitive impairment (MCI), fronto-temporal dementia (FTD), Gilbert's syndrome, Guillain-Barre syndrome, stroke, neuromuscular disease (NMD), facioscapulohumeral muscular dystrophy (FSHD), pervasive developmental disorder, frontotemporal lobar degeneration (FTLD), progressive supranuclear palsy (PSP), multiple system atrophy (MSA), motor neuron disease (MND), spinocerebellar ataxia (SCA), Huntington disease, muscular dystrophy, acute spinal cord injury, Cushing's syndrome, multiple myeloma, disseminated sclerosis, neurosyphilis, intrathecal tuberculin meningitis, delirium, aging, neuromuscular block, paralytic illness; loss of consciousness, cerebrovascular disease, stroke; cancer [mouth (oral squamous cell carcinoma, esophagus, nasopharynx);

thyroid; lung; breast; intestine (diarrhea, ulcerative colitis, colon, rectal, gaster, pancreatic); liver (hepatoblastoma, hepatocellular carcinoma, langerhans cell histiocytosis); kidney (Wilms tumor, renal cell); gallbladder; bladder (urothelial carcinoma); reproductive organ [uterus, cervix, ovarian, prostate, testicular]; bones (Ewing sarcoma, osteo sarcoma); tissue (rhabdomyosarcoma); blood [leukemia, lymphocytes (Hodgkin lymphoma), lymphatic system (non-Hodgkin lymphoma)]; poisoning (lead, organophosphate, pesticide, soman, snake venom, toxicity); other (apoptosis, postoperative outcome, pregnancy, solid malignancy, malign pleural effusion).

### 2.3.4 Materials and methods

Literature collection included systematic searches and research through platforms [NCBI, Medline, PubMed, OVID SP, EMBASE, Google Scholar database, Web of Science, SCOPUS, Cochrane library], usage of keywords (ex. bladder cancer, detection/diagnosis, biomarker assay) for literature review, systematic and mini review. Statistical analyses include tests and software usage. The most prevalent software from selected publications (70% out of total selected articles) is SPSS, STATA, SAS, R, GAMLSS, MATLAB, PLOT, STATISTICA, GraphPad PRISM, StatView, MedCal Software and Microsoft Excel (2008, 2013). By contrast, less common statistical software (30% out of the total selected articles) from the publication were: discriminator function analysis, PASW, MINITAB, SIGMA STAT, JMP, GENE Spring, GMDR, ORIGIN and PASW. Trends of the statistical analysis vary in selected publications. The surge of statistical analysis (85% out of total selected articles) included descriptive statistics, regression (multiple, multivariate, linear, quadratic, log, bivariate, binary, Poisson, Box-Cox transformation), Pearson correlation, exact test, LMS method, *T* test (independent sample, student, unpaired, paired, two-tailed, one-sided, two-sided), ANOVA (one and two way, univariate and multivariate), mixed model multivariate analysis (MANOVA), post hoc (Turkey, Bonferroni's, multiple comparison tests, Kramer test),  $X^2$  test, odds ratio, Fisher's exact test, Mann-Whitney test, Kolmogorov-Smirnov test, Shapiro-Wilk test, Kruskal-Wallis test, Kaplan-Mayer method, Bland-Altman analysis, Friedman-Wilcoxon test, Cohen's Kappa coefficient, Leuven test, power analysis, log-rank test, pairwise comparison test, hazard ratio proportional model. Less common statistical methodology in a publication (15% out of total selected articles) include Z score, relative standard error (RSE), McNemar-Bowker test, Friedman test, first-order confirmatory factor analysis (CFA), Hotelling's  $T^2$  test survival analysis, linkage disequilibrium, Scheffe post hoc, conditional logistic model, Cochran's and Q Higgins test, Harris-Benedict test, Mifflin St Jear

test, Mauchly's test, Dunnett's method, Newman-Keuls post hoc test, progression-free survival, tumor-specific survival, Dunn's multiple comparison test, Kawasaki and Tanaka's equation, Owen equation, Duncan's multiple range test, partial least squares, the net reclassification index (NRI), concordance correlation coefficient, proportional hazard and Weibull assumption, log-log survival curve, Cuzic's test.

### 2.3.5 Aims and conclusion

The selected majority of articles are focused on establishing healthy and disease reference values and assessing parameters as a gold standard in clinical and scientific research. Summarize the effect and importance of short and long-term physical activity, hydration/dehydration on health status. Investigate the consummation effect of supplements, alcohol, smoking and drinking. Emphasis was to discuss: current and potential biomarkers, the physiological and biochemical mechanisms of the health, disease and mortality state. Compare parameters based on gender differences and evaluate data accuracy. Examine the clinical significance of interventional trials and report the successfulness of therapy. Published articles debate the current methodology in clinical practice. Question and determine the most suitable method regarding cost, sensibility and specificity. Offer standardization protocol and methodology refinement; discuss the strengths, weaknesses and missing elements in the current literature. Provide possible goals for future research.

Selected studies created information conclusion bulk. Conclusions covered clinical relevance, hydration/dehydration, physical activity, disease, therapy and methodology. Identify risk factors for the non-homeostatic state of the organism. Data from diverse ethnicities and genders at the individual and population levels are collected. Results and administrative data are connected to medical services to enrich the dataset and facilitate cross-center sharing. The systematic and practical methodology is reproducible in larger datasets, sensitive, specific and applicable in routine monitoring. The state of hydration/dehydration has diverse effects on human health. Dehydration causes a loss of short-term memory and attention. By contrast, rehydration alleviates fatigue, improves attention and short-term memory. Coconut water has a better effect on cognitive performance as compared to plain water. Hydration status is associated with BMI. Additional fluid intake reduces BM loss and thirst sensation, and increases the risk of BM gain and gastrointestinal discomfort. Physical activity is physiological stress to a healthy organism. Faster runners lose BM when they drink less fluid. The dehydration state during the match is worsening in physically active individuals. Aerobic

exercise improves the ability to use oxygen and defense mechanism. It is a powerful therapeutic tool to help delay, prevent or treat cognitive decline in ageing individuals. Enhance brain function, attention, mood and stress resistance.

Physiological and hematological parameters vary based on training intensity, duration and frequency. Distance runners (13–97 km per week) have hematological parameter fall (Hg, Ht, MCV, MCHC, MCH, bilirubin, iron and ferritin). World-class distance runners develop anemia as a consequence of Hg decrease. Regular aerobic exercise has a beneficial effect in obese patients by reducing of endothelin-1 (ER-1) molecule. Moderate-intensity aerobic exercise augments endothelium-dependent vasodilatation, increases the production of nitric oxide and increases oxidative stress. A strong correlation exists between high-intensity training and inflammatory signaling. Oral supplementation modulates inflammatory signaling associated with exercise, reduces over-expression of pro-inflammatory cytokines and increases anti-inflammatory cytokines limiting the detrimental, pro-inflammatory strenuous exercise. Supplementation does not decrease RBC, Hg, Ht, NO and EGF signaling during exercise, expressing a pro-angiogenic effect. Improve nutrients, oxygen and muscle recovery after strenuous exercise.

Urine biomarkers are an advantageous noninvasive monitoring system. Urine biomarkers can be affected by diet, dehydration, medicines, physical activity and other factors. The presence of proteins, acids, creatinine, RBC, WBC, bacteria and crystals can indicate acute kidney injury, kidney stones, urinary infection, pregnancy. Changes in investigated blood factors are associated with disease pathophysiology and progression management. Values have an impact on clinical practice. Blood factors are useful prognostic and predictor markers of the disease. Examples are cognitive decline (albumin/globulin ratio or anemia); dementia (high-density lipoprotein, vitamin D, folic acid, cholesterol, HgA1c and LDL); AD (APOE  $\epsilon$ 4, anemia complications, serum copper and ceruloplasmin level); mania (low-grade inflammation, haemodilution and thyroid function abnormalities); euthymia (high-grade inflammation, haemodilution, thyroid function abnormalities due to HPA axis and autonomic deregulation); cancer (albumin/globulin ratio, postoperative survival for colorectal, lung cancer); anemia and malignancies (age, male sex, Ht and MPV); malnutrition (high sodium and low potassium); cardiovascular disease (ischemic heart disease\_increase MPV; coronary artery disease (CAD) and stenosis patients\_ blood hyper-viscosity and hyper-aggregation of red blood cells); Human T cell leukemia virus type 1 (Ly, anemia, decrease Eo and elevated lactate dehydrogenase levels);



postmenopausal women (low Hg, high RDW and PDW in comparison with premenopausal survival women). Air pollution caused by grilling (smoked fish processing) decreases the value of lymphocytes. Increase Hb, ER, HCT, MCV, MCH, MCHC, LE, PLT, RDW and Ne. Cholinesterase activity applies for assessing exposure to pesticides and health status, determining the severity of the disease and diagnostics cost-effectively. CSF sample is a tool for following disease progression and activity in neurological disorders, guiding outcome assessments and prognostic decisions in clinical trials. The rise of  $\gamma$ -globulin is associated with a Ly count increase in neurodegenerative diseases. Saliva biomarkers apply for clinical diagnosis of oral and systematic diseases, disease monitoring, management and decision making. Saliva is a noninvasive and accessible biofluid. The goal of therapeutic articles was to improve patient survival and quality of life by alleviating symptoms and disease eradication. Develop molecules, nanosensors and antioxidative supplements that target multiple factors and affect potency and disease pathophysiology. Implementation benefits include functional outcomes.

The development of screening routine tests enables early diagnosis and reduces survival rates associated with later detection and disease treatment. The methodology should be simple, low cost, highest precision and accuracy, sensitive and objective, with minimal time consumption.

### 3 Reference range of enzyme AChE

Additional file 2 contains additional minor publications revised regarding the establishment of reference range to investigate the influence of chemical and biological agents on disease onset and normal range in healthy participants. Included participants number in the study was from 1 to 1800 participants. For WB, PL and ER samples, the AChE range appoints.

The diverse experimental methodology applies to the analysis of blood samples. The most commonly used was the method by Ellman et al.

The range of AChE values of healthy individuals in ER samples is 2200–20000 U/L. In PL samples, AChE ranges from 1700 to 2110 U/L, and in WB samples from 2400 to 5000 U/L. In serum, AChE activity ranges from 2053 to 7100 U/L or 502.5 nmol/min/ml. In diseased individuals and individuals exposed to chemical agents, the values are varied. In the last 5 years (2016–2021), publications on healthy individuals and the Ellman method used to determine the value of AChE in the blood indicate a range of AChE activity that is significantly different from the range that exists in publications during the 1949–2021 year. AChE activity in healthy individuals ranges from 9594 to 11466 U/L in WB, 5320–12920 U/L

in PL samples, and 2027–8854 U/L in ER samples. More detailed information is available in Additional file 2.

### 4 Discussion

No clear evidence exists between journal publication and information quality. Based on the above results, literature content provides small functional usefulness of presented data comparing to the total number of published articles. Usually, the title and content miss keeping brief. A practical discussion is absent. Some of the papers miss responding to the earlier identified research questions. The solution to this problem would be to summarize concise information, key arguments and ideas. Evaluate research results and reduce the amount of less important information. Systematic investigation, research development, testing and evaluation develop or contribute to gaining new knowledge [18]. Some of the selected published journals show less successful argumentation in communicating ideas effectively. There is a lack of clarity, concision and uniformity of presenting ideas. However, others ease the interpretation of ideas, express persuasiveness and impede successful communication of well-selected data. Guidance regarding writing style and visual display of the results is respected, so science is more accessible to the audience.

Results are discussed in the past tense rather than in the present tense. This format helps distinguish new data from the previously reported. Helper words evoke an emotional tone or hide the meaning of an upcoming sentence. Helper words refer to like remarkably, interestingly, surprisingly. Quantity words regard to abundance, amount, significant, substantial and considerable. Word quantity aims to persuade, not to convey the information. Implicating and overstating the importance of presented data will not make the readers believe in the novel information. Some of the published papers contain jargon or commonly known abbreviations for better word description [19].

The consistency of new findings in some of the presented data is lacking. Footnotes are not included in papers to add clarity and uniformity to the data. Visual display of the results varies regarding value and impact on the scientific community. Graphs and tables present results. Choosing the best format for getting the intended message is significant for the interpretation of data quality. For example, presenting numerical data in graphs will lose precise values, which the table can provide. Some authors are more or less successful, depending on their expertise [18]. The inconsistency of the statistical results exists. Authors focus on p values that do not match the reported value and degree of freedom. The consequences are enormous. Increase of poorly based arguments the fallacious conclusion of observed effects, meta-analysis

bias and effect size estimate. All this can affect the reputation of an entire discipline [20]. Publish research results are significant to validate and to create novel solutions to a complex problem. However, there is a need to present consistent information of findings concisely and logically [18].

The most common topic of selected papers includes anthropometry with broad applicability and implementation as a noninvasive marker in clinical practice. Custom journals for publication were Plos One and Scientific Reports. The frequent publisher is Elsevier and Springer Nature. This information agrees with the study reported in literature [1, 20, 21]. Observational study types were the most prevalent in journals. Term observational describes a range of study design cross-sectional, case-control, prospective and retrospective cohort studies [22]. The difference is time, cost, differentiation between cause and effect, identification of predictors and outcome, odds ratio calculation, risk factor estimation, exposure status and reliability [23]. The main problems of observational studies are the presence of confounder and selection bias [24]. However, advanced statistical tools enable reliable control over many confounders [25]. The strength of the study is applicability in clinical practice, price and analysis speed. The observational studies address clinical questions (randomized clinical trials, exposure under the control of investigator), monitor long-term adverse events, assess whether clinical trial finding applies to a different population, provide preliminary data to justify the performance of a clinical trial as well as safety and benefits of approved medications [26–28]. The European continent is the most frequent in publishing selected journals, while Asia and America are not far behind. Europe had the most prevalent number of publications in the UK (7.1%).

In the Asian continent, China (5%) and Japan (3.6%) are the most common country for publication. By contrast, the American continent showed the highest incidence in the USA (14.5%) and Brazil (5.6%). These results support the finding that Europe produces the highest amount of world papers. From 2003 to 2018, the number of publications increased from 1.2 million to 2.6 million, showing 2.1 fold increases in the number [29]. However, based on other studies, the American continent is a global leader in published articles. Asia and the Republic of China are in second place [1, 30, 31]. North America and Canada published more than 60% of the scientific articles [32]. In 2014, the USA and China produced 19% and 17% of published papers. The countries like Germany, India, Japan and the UK, with 4 and 5% of total publishing, are observed [33]. At the moment, there is an existence of an increasing number of collaborative publishers from diverse continents [30].

The trend of publishing academic journals increases every year at a different rate. Here, we take a look at article publishing incidence from 1913 to the 2020 year. Suddenly grow of the selected publication started in the 1999 year. A rise in the number of journals is confirmed. Countries of one continent match the prevalence of this study. There is an increasing number worldwide of conference proceedings, open access archives and publications with differences between fields [1, 33–38]. Other authors state that journal growth rates have been remarkably consistent over time, with an average of 3.46% from 1800 to the present day [39–41]. The most common journal publisher type was Elsevier and Springer [42]. The health status of the participants in the study varies. Almost 50% of the selected publications contained information about disease participants without healthy control. Few studies showed not stated information regarding health status. Usually discussed diseases ranged from malnutrition, inflammation, cardiovascular disease, neurodegeneration and cancer.

The most common sample type in the literature was blood and anthropometry. General information about the participants (life habits, genetics and occupation) includes in the personalized questionnaire. Information regarding height, body weight and circumference, body mass and skin fold is in the anthropometry parameters. The majority of blood parameters contain information regarding hematology and biochemistry parameters. Urine parameters include information about urine content. Other parameters, from tissue, saliva, CSF, tears and sweat, were assessed in minority cases. The number of participants varies in an immense range, starting from one to a few million participants. An essential part of every study is the sample size and study population. The sample size reduces probability error, enables ethical standards, defines logistics and improves the success rates evaluated by funding agencies. It is an indispensable step for planning scientific studies. The absence of standardized participant numbers can harm study productivity and conclusions. Small sample size will not be able to provide a demonstration of desired difference and frequency precision. However, a large sample size adds to the study complexity, cost and feasibility. Both situations are ethically unacceptable and avoided by the investigator [43]. The participant age ranged from 0 to 100 years depending on the study information, usability, strengths, weaknesses and expected data. A disparity of conclusions comes from participant age [44]. Usually, applicable platforms for data collection were NCBI, Google scholar database. The most prevalent software was SPSS, STATA and SAS. The simple statistic was the most common (normality test, regression and *t* test). Sporadic papers contained wrong statistical tests and incorrect interpretations of

the results. Results consisted of text, tables and graphs. Research questions and study objectives were a match in the final article selection. In some publications, a lack of meaning and clarity of the presented data exist. Some of the results presented continuous data in small sample size studies. Other rarely included scattering plots, box plots and histograms to allow the reader to assess the data information. Figures display a large amount of data. Data are presented as mean $\pm$ -(SD) or mean $\pm$ -(SE), although (SD) and (SE) can give a different visual impression. The message is better conveyed by figures, enhancing critical thinking, discussion and understanding. These conclusions are following publication [45]. Microsoft Excel allows an easy, fast and efficient way to create bar charts. The software enables the analysis and representation of complex data (scatter plots, biological networks) [46, 47]. The selected publications aimed to establish a reference range of investigated parameters in health and disease. Summarize effects; determine differences, relations and validation of already established sweep. Discuss current and potential biomarkers, physiological and biochemical mechanisms, compare gender differences, determine the prognostic role and implement them as a diagnostic and predictive marker. Review current methodology regarding cost, sensitivity, specificity, standardization protocols. Define strengths and weaknesses and missing elements in the literature. The purpose of the conducted research was to overview basic principles and intellectual creativity, solve social problems, respond to social demands and contribute to the creation and development of science. Objectives were to conduct cutting edge research and international high-level science, globalize research and education. Discover new phenomena and create new technology. Provide future scientific suggestions based on academic foundations and vision. Raise the researcher level of excellence; promote corporatization and commercialization of results. Develop a performance evaluation system to encourage research activities [48]. Conclusions cover clinical relevance, reference range, hydration/dehydration, physical activity/inactivity, disease biomarkers, methodology and therapy. Identify genetic background, risk factors and variable range changes at the individual and population level. Conclusions regarding anthropometry, cognitive performance, memory and attention arose from hydration/dehydration studies. Physical activity causes variations in hematological and biochemical parameters during health and disease. It is a useful therapeutic tool to delay, prevent and treat cognitive decline, enhance brain function, attention and mood. Disease characteristics and molecular mechanisms are associated with sample biomarkers. Disease diagnosis, stratification, pathophysiology and progression are used for therapeutic monitoring and developing

drug strategies. Generating efficient molecules (inhibitor, supplements) enables efficient treatment, patient survival and quality of life improvement. The selected methodology is simple, low cost, accurate and sensitive with minimal time consumption. Discrepancies of hematological parameters in health and disease exist. Study findings and conclusions have a different point of view in comparison with already established information.

To generate new information, scientists apply concepts, explanations, arguments, models and facts. Manipulate, test, explore, predict, question, observe and make sense of the natural and physical world. Develop systematic knowledge through the learning experience and reflect the diversity of perspective. Engage researchers physically, emotionally and cognitively. Directly interact with the phenomena. Provide multifaceted, dynamic portrayals of science and build learner (reader) prior interest. The utilization of informal science learning enhances the learning experience and research results [49]. The majority of papers inform scientific ideas critically. They are high readable, state the most important outcomes, interpret findings at a higher level of abstraction, perspective and clarity. State idea about the issue addressed in the paper [50]. Different ways of presenting data and the refereeing process is a philosophy of success. Discuss all the significant factors like hypothesis testing, research cycle, experimental design, identifying sources of error, reducing the errors, data quality control check, data implementation, avoiding similar conclusions and frauds.

AChE reference range publications in the last 5 years significantly differ due to population, method sensitivity and laboratory settings differences. Results indicate the difference and progress of scientific information in twenty-first century. The manuscript aims to reuse old and create new functional knowledge. Make writing competitive and amusing to the scientific community. Contain information, objectives, descriptive of work and deliverable parameters. Results of the literature review are dynamic, innovative and cutting edge. A dedicated and enthusiastic search serves as an indicator for further analysis and strategic experimental planning in the field. Cover the topic complexity. Important aims and conclusions arose from the intensive data collection. The strength is the reduction of literature search and time. Prevent duplication efforts. Obtain texts with coherent arguments by rewriting, restructuring and rethinking. The limitation includes the absence of all used clinical parameters reference range and determination of  $p$  trend value. Publications were collected only once, without the update and may lead to less information gain. Other publications may be left unprocessed. The manuscript direct thinking assesses quality control, reuse old and implement new knowledge. Utilize innovative, problem

solving, logical, critical skills for developing self-confidence in own judgment. Logic, intuition, analysis, deduction, reasoning, observation and objectivity apply for information selection, hard work and the right philosophy. Research knowledge justifies with evidence.

## 5 Conclusion

Descriptive review results raise conceptual issues suited to professionals in the field. This study focuses on key findings, interpretation, methodology, habitual ideas and concepts through a quantitative and qualitative approach. Identification of problems, key points, and research gaps are critically assess and discuss. Readers have an idea of achievements in the field and areas of question and debate. The publication is consistent, systematic with logical structure, well written, focused and critical. This study is essential and beneficial for further research development. The research will be able to put existing data into use (project or commercially). Avoid laborious time consuming for data finding and gain necessary knowledge (thoughts, ideas about the project techniques) about the topic. Establish valuable future collaboration. Discover and connect the dots of information. It will allow the reader to emphasize the evidence and widely apply knowledge of gaining theoretical and practical experience and organize discussion clubs for students and colleges. Convey the newest information in science from literature. Provide good counseling for study participants. Guide them through the process of assessing risk and determining what screening they need for further studies.

## Abbreviations

ALS: Amyotrophic lateral sclerosis; AD: Alzheimer disease; ASMI: Appendice index skeletal mass; ALM: Appendice lean mass; ALMI: Appendice Lean Mass Index; ADI: Abdominal diameter index; AMA: Area arm muscle; AFA: Area arm fat; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; AMT: Aminomethyltransferase; AChE: Acetylcholine esterase; Al: Aluminum; Abeta: Amyloid beta; ANOVA: Analysis of variance; A: Albumine; AD: Alzheimer disease; APOE ε4: Apolipoprotein E4; AchRs: Acetylcholine receptor; AChE: Acetylcholine esterase; AMC: Anthropometric measure chair; ABSI: A body shape index; ALSTI: Appendicular lean soft tissue index; BM: Body mass; BMI: Body mass Index; BWL: Body weight loss; BWC: Body weight change; BF: Body fat; BSI: Bone strength index; BAI: Body adiposity index; BHR: Bust to hip ratio; BMR: Basal metabolic rate; BUN: Blood urea nitrogen; BChE: Butyrylcholine esterase; BA: Basophil; Ba: Barium; Bo: Boron; Br: Bromide; CSF: Cerebrospinal fluid; CRP: C reactive protein; CST: Static lung compliance; Ca: Calcium; CO<sub>2</sub>: Carbon dioxide; ChE: Cholinesterase; CD: Cluster of differentiation; CEA: Carcinoembrionic antigen; CL: Chloride; Co: Cobalt; Cu: Copper; Cd: Cadmium; Cs: Cesium; CEA: Carcinoembrionic antigen; chit-1: Chitinase 1; CL: Cochrane library; CI: Confidence interval; DLM: Dry lean mass; DA: Discriminator function analysis; EO: Eosinofil; ER: Erythrocyte; ECW: Extracellular water; FFM: Fat-free mass; FMI: Fat mass index; FFM: Fat-free mass index; FM: Fat mass; FAMA: Forearm muscle area; FTL: Frontotemporal lobar degeneration; FSHD: Facioscapulohumeral muscular dystrophy; FFA: Fat-free fat acid; Fe: Ferrum; FTD: Frontotemporal dementia; FI: Foot Index; GS: Gilbert's Syndrome; GSD: Google Scholar database; GAMLSS: Generalized additive model for location, scale and shape; GMDR: Generalized multifactor dimensionality reduction software; G: Globulin; GFR: Glomerular filtration rate; H: Height; HC: Hip circumference; Hg:

Hemoglobin; Ht: Hematocrit; HR: Heart rate; HCO<sub>3</sub>: Sodium bicarbonate; HDL: High-density lipoprotein; Hg: Hemoglobin; Ht: Hematocrite; Hg: Mercur; HIV: Human immunodeficiency virus; HTLV-1: Human T cell leukemia virus type 1; HgA1c: Hemoglobin A1C; IL: Interleukin; Ig: Immunoglobulin; IFN-gama: Interferon gama; ICW: Intracellular water; J2: Iodide; JMP: Statistical software; K: Potassium; LMM: Lean muscle mass; LBM: Lean body mass; LCM: Load capacity metabolic indices; Li: Lithium; LMS method: Lambda-Mu-Sigma; LDL: Low-density protein; LDL: Low-density lipoprotein; LY: Lymphocyte; Le: Leucocyte; MM: Muscle mass; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean cell volume; MCS: Mental component summary; MAMA: Mid-arm muscle area; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MPV: Mean platelet volume; Mn: Mangan; Mg: Magnesium; Mo: Molibden; MO: Monocyte; Mn: Mangan; MAPK: Mitogen-activated protein kinase; MIP-1alpha: Macrophage inflammatory protein-1alpha; MCI: Mild cognitive impairment; MSA: Multiple system atrophy; MND: Motor neuron disease; MANOVA: Mixed model multivariate analysis; Mg: Magnesium; MPV: Mean platelet volume; NCBI: National Center for Biotechnology Information; NMD: Neuromuscular disease; Na: Sodium; Ni: Nickel; NRG-1: Neuregulin 1; NE: Neutrophils; NMP: Nuclear matrix protein; OR: Odds ratio; P: Phosphorus; PASW: Predictive analytics software; PSP: Progressive supranuclear palsy; PK: Protein kinase; Pa: Protactinium; PLT: Platelet; RBC: Red blood cells; Re: Rhenion; Se: Selen; Si: Silicon; SCA: Spinocerebellar ataxia; SPSS: Statistical Package for the Social Sciences; SAS: Statistical analysis software; SD: Standard deviation; SEL: Stature elbow length; SSH: Stature shoulder height; SADH: Abdominal sagittal diameter to height; SMI: Severe motor impairment; STM: Brain (short-term memory); STM: Soft tissue mass; SM: Skeletal mass; SNCA: α-Synuclein; TR: Trombocite; TBSM: Total body skeletal mass; TBSMI: Total body skeletal mass index; TFM: Truncal fat mass; TSH: Thyroid stimulating hormone; TNM: Tumor, node, metastasis; TBW: Total body water; UK: United Kingdom; USA: United States of America; VEGF: Vascular endothelial growth factor; Zn: Zinc; W: Weight; WC: Waist circumference; WHR: Waist to hip ratio; WHtR: Waist to height ratio; WSR: Waist stature ratio; WBC: White blood cells; WOS: Web of Science.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12301-021-00239-6>.

**Additional file 1.** Reference list of selected literature (982 papers) for data extraction and analysis.

**Additional file 2.** Enzyme AChE reference ranges from the literature.

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## Authors' contributions

SJ originated the study idea, paper and data collection, analysis, interpretation and writing the manuscript. SJ read and approved the final manuscript. SJ confirmed that this work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere. The author read and approved the final manuscript.

## Authors' information

Snežana Jovičić, a student, is born on 17-10-1990 in Belgrade, Serbia. She finished two high schools, Medical and Musical high school. Academic qualifications: enrolment of Ph.D. studies, Genetics (2014). Snežana Jovičić completed M.Sc. Human Molecular biology, (2014) and B.Sc. Molecular Biology and Physiology (2013). Snežana is a hardworking, creative, communicative and charismatic person, capable of working in diverse situations, effectively managing time. Adore solving complex intellectual problems and communicating with distinct personalities. During free time, Snežana involves in activities such as swimming, rollerblades, playing violoncello, singing, classical music, walking, dancing salsa and Latin dances. Moreover, she spends free quality time with family and friends. A significant part of everyday life is to



work on personal and professional development, reading books in psychology, archeology, art, travel and meeting new people, cultures and ways of living. Areas of scientific interest are related to human diseases (cancer, inflammation, immunology and cardiovascular diseases), activation of molecular pathways, gene expression, clinical studies, pharmacovigilance, connecting medicine and science, academic reading, writing, data analysis. Personal interest is linked to the increasing quality of human healthcare and creating widely applicable knowledge.

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#### Availability of data and materials

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#### Ethical approval and consent to participate

Not applicable.

#### Consent for publication

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#### Competing interests

The author, a Ph.D. student, Snežana Jovičić, declares no competing interest.

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