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Review Article

The Use of Biomarkers in Research with Nursing Personnel: A Narrative Review

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Abstract

Objective: To analyze studies with nursing personnel, with the use of biomarkers as an investigation method for the detection of health alterations. **Method:** This is a Narrative Literature Review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology. The PICO strategy was used in this review's development. For the search in databases and virtual libraries, the descriptor "Biomarkers" and the keywords "Nursing Personnel" and "Health Changes" were used in Portuguese, English, and Spanish. The search was carried out in scientific databases and articles related to the theme, published from 2002 to May 2022.

Results: From 19 articles analyzed, it was found that the use of biological markers allowed the detection of problems such as higher values in capillary cortisol levels in a group of nurses with burnout when compared to those without burnout; cortisol levels on waking hours associated negatively with the number of years working and positively with damage to their DNA; occupational exposure to anesthetic gases that influence hepatic and renal hemochemical parameters in those exposed; iron-deficiency anemia and different thyroid gland diseases prevalent among nurses when compared to those of controls matched by sex and age, chromosomal aberrations, and so forth.

Conclusion: In general, if biomarkers assist in the identification of alterations in the health of nursing personnel and enable a significant contribution to occupational health and safety, a more holistic approach will be needed to transfer them from the laboratory to professional practice, especially to be used as a tool in the management of occupational health.

Introduction

In the health area, the nursing team personnel perform their work, represented by the care provided to patients, in a systematized and hierarchical format. These activities include care provided directly to patients, as well as tasks related to teaching, service management, research, and leadership of teams and health systems [1]. During their experience in the workplace, this team can become ill due to the nature of the tasks they have to perform [2,3], the frailties and deficiencies that can be associated with the organization and working conditions, such as work overload, long working hours and stress [4], among others. Scales or inventories, clinical evaluations, and/or others are instruments that can be used to identify illnesses, work overload, and biological alterations that labor activities can cause in the workforce [5]. Qualitative studies also use interviews or observation techniques to obtain data and analyze them, according to the various theoretical and methodological references used. However, another way to identify the possible causes of health alterations in the workforce, still underused, is the use of biomarkers or biological markers, obtained from biological organic samples, which are considered potentially useful tools for research, practices, and policies of occupational health and safety [6]. They can be diagnostic tools that discriminate between health and disease states and are also known as biological indicators [7]. Biomarkers are therefore substances or their biologically transformed products, as well as early biochemical alterations, whose determination in biological fluids, tissues, or exhaled air can evaluate the intensity of exposure and the health hazards [8]. They can be objectively measured and evaluated as indicators of normal or pathogenic biological processes, or they can be pharmacological responses to certain therapeutic interventions [9]. The mechanisms of their release in the presence of mental phenomena, such as depression, anxiety, anguish, and suffering, among others, are still being studied; they are predictive tests for screening and support in the diagnosis of some pathologies, such as mental disorders. Their use comprises a search and surveillance strategy in health [10].

In recent years, research using biomarkers as a method of disease investigation has become established as an indicator of great potential for identification and diagnosis [11]. When used in isolation or in conjunction with self-reported health assessments, for instance, through the use of psychometric scales, cardiovascular, metabolic, inflammatory, neuroendocrine, and other biomarkers have been shown to be predictors of mortality and morbidity [10]. The early identification and diagnosis of a health alteration can have a direct impact on the treatment and prognosis of several pathologies. Therefore, the use of strategies that perform this detection or even the tracking of diseases is of utmost importance, and among these detection strategies is the use of biomarkers. In many cases, it is possible to find signaling molecules or particles of health alterations [12]. These organic samples can assist, for instance, in the identification and quantification of occupational hazards through the biological assessment of human exposure [6]. They aim to measure the hazards derived from exposure, not only by the presence of the agent in the environment - in greater or lower concentration - but as a function of the amount that was actually absorbed by the body. They can be obtained in various body fluids, such as saliva, urine, blood, tears,



and tissues [13]. They include almost any measurement that reflects the interaction between a biological system (blood, saliva, hair, fingernail, urine, feces, among others) and an environmental agent, which may be chemical, physical, or biological [6]. They can then be measured experimentally and enable the indication of the existence of a certain normal or pathological function of a given organism [7]. However, despite their importance and the possibility of identifying health problems in the workforce early and objectively, their use in research involving nursing personnel still seems to be limited. This reduced use possibly stems from the need to use laboratory equipment to perform the analysis, as well as kits, which are expensive in most cases and limit the implementation of these studies. In light of the question raised, the objective of this study was to analyze studies with nursing personnel using biomarkers as an investigation method to detect health alterations.

Method

To reach the proposed objective, a Narrative Literature Review was performed, which is a literature analysis to describe and discuss the development or the "state of the art" of a given subject, from a theoretical or contextual point of view, and may include published articles and books and/or chapters; the published literature is analyzed, in addition to the experience, interpretation and critical analysis of the review's authors [14]. It consists of a broad literature analysis, without establishing a rigorous and replicable methodology in terms of data reproduction and quantitative answers to specific questions; it updates the knowledge on a specific theme, highlighting new ideas, methods, and subthemes with little or no emphasis on the selected literature [15,16]. Thus, this review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology. This methodology is widely used in review studies (PRISMA Statement) [14]. The PICO strategy was employed in the development of this review and in the elaboration of the guiding question, considering P (Patients) = nursing personnel; I (Intervention) = use of biomarkers; C (Comparison) = not applicable; O (Outcome) = detection of health alterations.

Given the above, and considering the personal experience of the present study's authors, who are all nurses, this text was based on the following guiding question:

What is the scientific evidence on health alterations among nursing personnel detected through investigations that used biomarkers? For the search in databases and virtual libraries, the following Health Science Descriptors (DeCS) were used: "Biomarkers" in Portuguese (Biomarcadores), "Biomarkers" in English, "Biomarkers" in Spanish (Biomarcadores), and the keywords "Nursing Personnel" (Trabalhadores de Enfermagem) in the three languages, and "Health Alterations" (Alterações na saúde) in the three languages, interlinked by the Boolean operator (delimiter) "and". The texts, with these words/keywords, were searched in the virtual libraries Science Direct and Scientific Electronic Library Online (SciELO), and the database used was the Medical Literature Analysis and Retrieval System Online (MedLine) via Pubmed. The papers with at least two of the three determined descriptors/keywords that addressed nursing personnel were included, even when they were mentioned among "healthcare professionals". Those papers whose titles and abstracts failed to address biomarkers, included professionals other than nursing personnel or teams, or failed to address health alterations among this population, were excluded. The period determined for this search was from 2002 to May 2022. The titles and abstracts of all articles listed were reviewed and, if considered appropriate, were obtained and read in full. A list of articles to be included was made, including their objectives, methods, and main conclusions.

Results

In the Science Direct virtual library, the search yielded 164 articles; however, after reading the titles and abstracts, 3 (three) were identified as meeting the determined inclusion criteria. In the SciELO virtual library, the search yielded 3 (three) articles, but only 1 (one) was related to the theme; in the MedLine database, via PubMed, 22 articles were identified, which, after analyzing the titles and abstracts, resulted in 15 that addressed the proposed theme. That is, from a total of 189 articles, 19 were included in this study. To better understand the object covered in the present review, the following (Table 1) was prepared, which presents the titles of the articles, year of publication, database/virtual library where it was identified, the journal where it was published, authors and country of origin, objective, professionals involved, exams performed, the biomarker used in the study, and main conclusions.

Table 1: Distribution of articles on health alterations among nursing personnel detected by biomarkers, according to the study variables. 2002-2022 (n=19).

Table with 6 columns: Article Title/Journal/Virtual Library/ Database/Year of Publication/ Article Identifier, Authors/author's country of origin, objective, Personnel included, Biomarkers used, Main Conclusions. It contains two rows of data.



<p>Evaluation of stress, burnout and hair cortisol levels in health workers at a University Hospital during COVID-19 pandemic/ Psychoneuroendocrinology Volume 128, June 2021, 105213/Science Direct/2021/ https://doi.org/10.1016/j.psyneuen.2021.105213 [19]</p>	<p>Ibar C, Fortuna F, Gonzalez D, Jamaro J, Jacobsen D, Pugliese L, Giraudo L, Cereso V, Mendoza C, Repetto EM, Reboredo G, Iglesias S, Azzara S, Berg G, Zopatti D, Fabre B/ Argentina</p>	<p>To evaluate the stress and burnout in a population of healthcare professionals and to measure cortisol concentration in hair as a current stress biomarker.</p>	<p>234 healthcare professionals from a hospital in Buenos Aires were included in this study. The study population was divided into three groups, considering the following aspects: Individuals below the healthy reference range (< 40 pg/mg hair), within the healthy reference range (40-128 pg/mg hair), and above the healthy reference range (> 128 pg/mg/ hair mg).</p>	<p>Capillary cortisol measured by a chemiluminescence method.</p>	<p>40% of the studied population presented hair cortisol values outside the healthy reference range; in this entire population, a direct correlation was found between hair cortisol concentration and perceived stress, and between hair cortisol concentration and the emotional exhaustion component of burnout; 12% of the studied population presented burnout. Higher values in hair cortisol levels were found in the group with burnout versus individuals without burnout. Depersonalization is a mediating variable in the relationship between self-perceived stress and cortisol levels. Healthcare professionals are subject to increasing levels of stress and burnout. High depersonalization, emotional exhaustion, and decreased sense of personal accomplishment define this population. Health authorities should implement strategies to manage this psychological emergency.</p>
<p>Professional exposure to anaesthetic gases in health workers: estimate of some hepatic and renal tests/ Clin Ter. 2013;164(1):e5-9/Medline via Pubmed/ https://doi.org/10.7417/CT.2013.1513/ [20]</p>	<p>Caciari T, Capozzella A, Tomei F, Fiaschetti M, Schifano MP, Gioffrè PA, Santoro L, Scala B, Nardone N, De Sio S, Chighine A, Tomei G, Rosati MV/ Italia</p>	<p>To estimate whether occupational exposure to low doses of anesthetic gases can cause changes in hepatic and renal hematological parameters in healthcare professionals working in a local hospital.</p>	<p>154 exposed subjects and 98 unexposed controls; the exposed were divided into more exposed (group 1: n.54) and less exposed (group 2: n.100). Each professional included in this study underwent the Complete Blood Count (CBC) test.</p>	<p>Serum albumin, alpha 1, alpha 2, beta and gamma globulins, serum creatinine, and gamma-GT.</p>	<p>Occupational exposure to low doses of anesthetic gases can influence hepatic and renal hemochemical parameters in healthcare professionals exposed.</p>
<p>The state of health of oncology nurses characterized by genetic and immunotoxicologic biomarkers/ Magy Onkol. 2006;50(2):153-61. Epub 2006 Aug 4/Medline via Pubmed/ acceso em: https://pubmed.ncbi.nlm.nih.gov/16888679/ [21]</p>	<p>Tompa A, Magyar B, Tóth F, Biró A, Fodor Z, Jakab M, Major J/ Hungary</p>	<p>To evaluate the clinical, genetic, and immunotoxicological risk of nurses in oncology units in Hungary.</p>	<p>500 nurses, with evaluations performed during the last 10 years in oncology units in Hungary.</p>	<p>Genetic and immunotoxicological biomarkers, measurement of iron and serum glucose levels.</p>	<p>Iron-deficiency anemia and different thyroid gland diseases were more prevalent among nurses than controls matched for sex and age. Persistent iron-deficiency may increase serum glucose levels and thus the risk of diabetes. Among the genetic and immunotoxicological biomarkers studied, the frequency of chromosomal aberrations, sister chromatid exchange, and B lymphocytes were significantly increased compared to matched controls. The changes obtained demonstrate the occupational exposure of nurses to cytostatic drugs, and stricter hygienic regulations and compliance with European Union chemical safety standards are needed.</p>
<p>Biological risk and health care workers: analysis of the effects of work chronobiology on the immune system/ Med Lav. Nov-Dec 2010;101(6):427-36/ Medline via Pubmed/acceso em: https://pubmed.ncbi.nlm.nih.gov/21141454/ [22]</p>	<p>Copertaro A, Bracci M, Amati M, Mocchegiani E, Barbaresi M, Copertaro B, Santarelli L/ Italy</p>	<p>To compare the immune status of a group of shift nurses with that of nurses who work only day shifts.</p>	<p>A total of 138 nurses were evaluated at baseline and after one year of follow-up.</p>	<p>The number of lymphocytes and subpopulation of CD3+, CD4+, CD8+-CD57+, CD19+ and CD56+, cytotoxic activity and lymphoproliferative response of NK cells, serum concentrations of IL-1beta, IL-6, INFgama and TN Falfa were analyzed.</p>	<p>Perceived stress and daytime sleepiness tests were performed. No significant changes were found in any of the parameters studied both at the beginning and after one year of follow-up. The biological risks for nurses do not seem to be increased by shift work.</p>
<p>The plasma concentration of copper and prevalence of depression were positively correlated in shift nurses/ Biol Res Nurs. v. 16, n. 2, p. 175-181, abr. 2014 Medline via Pubmed/ https://doi.org/10.1177/1099800413479156 [23]</p>	<p>Chang MY, Tseng CHO, Chiou Ya-L / Thailand</p>	<p>To investigate the relationship of serum trace element levels with mental health and tendency to depression in shift nurses.</p>	<p>90 shift nurses (daytime, evening, and night shift) working in intensive care units.</p>	<p>AST, ALT, CRP, and uric acid inflammation markers. Plasma ferritin, cortisol, il-6, and TNF-α were measured; in plasma the concentrations of calcium, magnesium, phosphate, sodium, zinc, copper, and selenium were obtained.</p>	<p>Participants who worked the night shift presented mild to moderate levels of depression that were significantly higher than those in the control group; they also presented higher levels of plasma copper, ferritin, interleukin (IL)-6, and alanine amino transferase than the control group.</p>



<p>Assessment of the absorbed dose after exposure to surgical smoke in an operating room. Toxicology Letters, v. 328, p. 45–51, 1 ago. 2020 Science Direct/ https://doi.org/10.1016/j.toxlet.2020.04.003 [24]</p>	<p>Gestel EAFV, Linssen ES, Creta M, Poels K, Godderis L, Weyler JJ, Schryver AD, Vanoirbeek JA / Belgium</p>	<p>To evaluate surgical smoke and its contamination on staff members working in operating rooms.</p>	<p>15 professionals who had their urine samples collected.</p>	<p>Urinary S-phenylmercapturic acid (S-PMA), o-cresol, mandelic acid, and 1-hydroxypyrene were analyzed for biomonitoring benzene, toluene, and styrene, respectively.</p>	<p>Ambient air was assessed. O-cresol was elevated, but this was not clearly related to toluene exposure from surgical smoke in operating room personnel. Circulating nurses and cleaning assistants seem to be more exposed to surgical smoke than surgeons.</p>
<p>Assessment of Salivary Human Herpesvirus-6 and Immunoglobulin A Levels in Nurses Working Shifts. Asian Nursing Research, v. 2, n. 3, p. 159–165, 1 set. 2008 Science Direct/ https://doi.org/10.1016/S1976-1317(08)60039-0 [25]</p>	<p>Fukuda H, Ichinose T, Kusama T, Sakurai R/Japan</p>	<p>To evaluate whether salivary human herpes virus-6 (HHV) acted as a new stress-sensitive marker providing a reliable indicator of stress among shift nurses.</p>	<p>56 nurses who worked only the day shift and those who worked at night were divided into groups A and B.</p>	<p>Salivary HHV-6; immunoglobulin A (IgA).</p>	<p>Mood states were compared. The salivary level of HHV-6 may be considered a more sensitive stress marker than salivary IgA or mood to assess chronic fatigue in shift nurses.</p>
<p>A pilot study on the association between job stress and repeated measures of immunological biomarkers in female nurses. International Archives of Occupational and Environmental Health, v. 83, n. 7, p. 779–789, 1 out. 2010 Medline via Pubmed/ https://doi.org/10.1007/s00420-010-0544-0 [26]</p>	<p>Lee K-Mu, Kang D, Yoon K, Kim Sun-Y, Kim H, Yoon H-Suk, Trout DB, Hurrell Jr JJ/Korea</p>	<p>To evaluate the immunosuppressive effects of work stress on nurses at a university hospital.</p>	<p>Four groups consisting of ten nursing professionals.</p>	<p>White blood cell numbers and lymphocytic proliferation of mitogens and toxoid were measured by flow cytometry and radioimmunoassay; serum levels of hydrocortisol, IL-1β, IFN-γ, TNF-α, and salivary IgA were measured by an enzyme-linked immunosorbent assay.</p>	<p>The level of white blood cells was lower in the high objective stress group compared with the low objective stress group. In terms of immune biomarkers, the level of TNF-α was moderately lower in the high objective stress group compared to the low objective stress group, while the level of total IgA was significantly higher in the high objective stress group. Psychological work-related stress seems to have affected the levels of some immunological biomarkers in nurses.</p>
<p>The Influence of Light at Night Exposure on Melatonin Levels among Canadian Rotating Shift Nurses. Cancer Epidemiology and Prevention Biomarkers, 27 Sep. 2011 Medline via Pubmed//https://doi.org/10.1158/1055-9965.EPI-11-0427 [27]</p>	<p>Grundty A; Tranmer J; Richardson H; Graham CH; Aronson KJ/Canada</p>	<p>To evaluate the influence of nocturnal light exposure on melatonin levels.</p>	<p>123 nurses on a rotating shift (two 12-hour days, two 12-hour nights and five days off).</p>	<p>Melatonin obtained in saliva</p>	<p>Average light exposure was significantly higher when nurses worked at night, although peak melatonin levels and the daily change in their levels were similar across day/night shifts.</p>
<p>Biomarkers of end of shift exposure to disinfection byproducts in nurses. Journal of Environmental Sciences, water treatment and disinfection by-products. v. 58, p. 217–223, 1 ago. 2017 Science Direct/ https://doi.org/10.1016/j.jes.2017.06.031 [28]</p>	<p>Ioannou S, Andrianou XD, Charisiadis P, Makris KC/Cyprus</p>	<p>To identify the prevalence of exposure to disinfection byproducts, such as trihalomethanes (THMs).</p>	<p>179 nurses working in two public hospitals.</p>	<p>The prevalence of exposure to disinfection byproducts, such as trihalomethanes (THMs), was identified using self-reports and measurements of these biomarkers.</p>	<p>Nurses were exposed to almost twice the levels of THM when compared to values obtained in the general population. THM proved to be an effective biological marker for exposure to disinfectants used in hospitals.</p>
<p>Relationship of Job Satisfaction, Psychological Distress and Stress-Related Biological Parameters among Healthy Nurses: A Longitudinal Study. Journal of Occupational Health, v. 52, n. 1, p. 31–38, 2010 Medline via Pubmed/ https://doi.org/10.1539/joh.19042 [29]</p>	<p>Amati M, Tomasetti M, Ciuccarelli M, Mariotti L, Tarquini LM, Bracci M, Baldassari M, Balducci C, Alleva R, Borghi B, Moccigiani E, Copertaro A, Santarelli L/Italy</p>	<p>To investigate the relationship between job satisfaction, psychological stress, psychosocial processes, and biological factors related to stress.</p>	<p>115 nurses working in hospitals.</p>	<p>Blood samples for obtaining CD3, CD4, CD8, CD8-CD57 T lymphocytes, CD19 B lymphocyte, NK CD56 cells, and active NK cells were determined.</p>	<p>Reduced psychological stress was associated with job satisfaction and reduced numbers of CD8(+) - CD57(+) activated T cells and inflammatory cytokines. Psychological stress mechanisms affecting immune cell function were associated with job dissatisfaction.</p>
<p>Stress in nurses: the use of salivary cortisol in the working day and off. Journal of the USP School of Nursing, v. 47, no. 5, p. 1187–1194, Oct. 2013/ SciELO/ https://doi.org/10.1590/S0080-62342013000500025 [30]</p>	<p>Rocha MCP, De Martino MMF, Grassi-Kassisse DM, Souza AL/Brazil</p>	<p>To evaluate salivary cortisol concentration in nurses during working and off-duty days.</p>	<p>57 nurses</p>	<p>salivary cortisol</p>	<p>The salivary cortisol concentration identified the level of stress in nurses and the difference obtained between a working day and a day off; on the day off, the concentration remained at lower values, as did the stress score.</p>

In the articles included in this review, the years 2010 and 2021 were predominant (three studies in each), followed by 2013, with two articles. Regarding the authors' countries of origin, there was diversity, involving countries from the Americas, European Union, and Asia (**Chart 1**).



Discussion

From the studies identified and included in this review, the authors' concern with healthcare professionals and, in particular, nursing professionals, was noted. The work performed by nurses requires technical and cognitive abilities and competencies for its development [31], some characteristics related to the nature of this work, such as working hours, workload, pressure from peers and superiors, alternating shifts, interpersonal relationships, among others, can negatively impact the physical and mental health of these professionals [32]. Back pain, musculoskeletal diseases, cancers, heart diseases, weight alterations, and sleep disorders seem to be common elements in this population [33], in addition to mental health alterations such as fatigue, burnout syndrome, depression, anxiety, and, consequently, changes in the quality of life [34], among other problems. These professionals may find themselves stressed, exhausted, suffering for the work they do, disappointed because their professional ideals are often not achieved; their work environments may be inadequate, how work activities are organized, little appreciation for the professional, unsatisfactory participation in work decisions, excessive demands, alternating shift schedules, low wages, performing work that is inconspicuous and complex, among other factors, including undesirable conditions, with occupational risks, may favor illnesses in these professionals [35]. The use of biological markers in the studies identified by the present review enabled the detection of some of these problems, such as: Higher values in hair cortisol levels were found in the group of nurses with burnout when compared to those without burnout [19], cortisol levels at waking hours were negatively associated with the number of years a nursing professional had worked and positively with damage to their DNA [17], the frequency of chromosomal aberrations, sister chromatid exchange, and B lymphocytes was increased among nurses when compared to matched controls; such changes demonstrate nurses' occupational exposure to cytostatic drugs [21], hair cortisol was shown to be outside the healthy reference range [19], occupational exposure to low doses of anesthetic gases may influence hepatic and renal hemochemical parameters in exposed healthcare professionals, including those in nursing [20], iron-deficiency anemia and different thyroid gland diseases were prevalent among nurses when compared to controls matched for sex and age [21], depersonalization is a mediating variable in the relationship between self-perceived stress and cortisol levels, and healthcare professionals, including those in nursing, are subject to increasing levels of stress and burnout: Therefore, high depersonalization, emotional exhaustion, and a decreased sense of personal accomplishment characterize this population [19], among other problems.

Nursing has as its core activities the care and/or assistance to human beings and, in this sense, there is a close connection between work and the professionals, since the agent of nursing work and the subject of the action is the human being. And in this relationship, joy, sadness, suffering, pleasure, satisfaction, and dissatisfaction may occur, which, added to how the work is performed and its organization, end up favoring physiological alterations in the nursing professionals' bodies, which may affect their health and, consequently, affect them with several health problems. The physiological mechanisms associated with the work environment can adversely affect the safety of patients under their care, in addition to the health of the nurses themselves [36]. With the increase in working hours, some phenomena may also occur, including physical and emotional wear and suffering in daily life. Added to the precarious working conditions, such problems can generate professional dissatisfaction, hinder interpersonal relationships within the public and private dimensions, and also compromise the assistance provided to patients [4].

Therefore, it is clear that the studies performed with biomarkers contribute, with greater objectivity and quality in the evaluations, to understanding the various health problems/alterations that affect nursing professionals. These markers can be obtained, for instance, in human saliva, which can reproduce the metabolic, nutritional, immunological, and hormonal status of an individual [37]. In it, it is possible to find more than 2000 proteins, and approximately a quarter of these are also identifiable in serum values. Such findings demonstrate the biochemical relevance of saliva, as a diagnostic possibility and health monetization strategy in humans [38,39]. A study sought to identify whether salivary human herpes virus-6 (HHV) acted as a new stress-sensitive marker to provide a reliable indicator of stress among shift nurses. The results showed that salivary HHV-6 level could be considered a more sensitive stress marker than salivary IgA or mood to assess chronic fatigue in shift nurses [25]. In a review study [6], the authors addressed the incorporation of salivary biomarkers in studies with nursing professionals. Thus, several analytes found in saliva may present potential interest for nursing research, and among such salivary biomarkers are the following: -Endocrine markers: Aldosterone, Estradiol, Estriol, Estrone, Androstenedione, Melatonin, Cortisol, Progesterone, Testosterone; -Inflammatory and immune markers: Interleukins IL-1, IL-2, IL-6, IL-8, Beta-2-microglobulin, Neopterin, C Reactive

Protein (CRP), Secretary Immunoglobulin A; - Those of the Central Nervous System: Alpha-amylase, Intestinal Vasoactive Peptide, and Neuropeptide Y; -The genetic ones: Bacterial Mitochondrial, Human Genome m RNA; -The antigen-specific antibodies: Malaria, Hepatitis A, Hepatitis B, Measles, Rubella, Herpes simplex, Mumps; Human immunodeficiency virus; -The pharmacological ones: Alcohol, Lithium, Cannabidiol, Caffeine, Phenytoin, Cocaine Opioids, Amphetamine, Methadone, Nicotine, and Bisphenol-A [6].

In Brazil, a study evaluated the concentration of salivary cortisol as a physiological index indicating the degree of stress in nurses on workdays and off-duty, correlating it with a Nurses' Stress Inventory (NSI). This research used socio-demographic data, the NSI, and salivary cortisol dosages. A total of 57 nurses participated (80.7% female, mean age 37.1 years); the mean NSI score was 124.5; the mean cortisol concentration was 564.1 ng/mL on workdays, and 354.1 ng/mL on the days off. Those who worked a double shift presented higher salivary cortisol concentration values on working days (638.1 ng/mL). It was concluded that the salivary cortisol concentration identified the level of stress experienced by nurses and the difference obtained between a working day and a day off; on the day off, the concentration remained at lower values, as well as the stress score [30]. The results of another Brazilian study corroborate the proposal of using salivary cortisol to assist in the tracking of deleterious conditions generated by chronic occupational stress in nursing professionals, contributing to the early recognition of these conditions and the adoption of preventive measures that allow the maintenance of the quality of care in health services [40]. A Brazilian study with nurses who worked in the emergency room, where salivary cortisol was obtained to measure stress, failed to find a correlation between workload and levels of occupational stress, physiological reactions from stress, and salivary cortisol levels [41]. Also, in Brazilian studies, salivary cortisol was obtained to evaluate stress among nurses with alternating shifts [42]. Chromogranin A was obtained in saliva to evaluate anxiety among hospital nursing professionals [43], among others. Another way to obtain biomarker values is from hair, a less aggressive technique than venous punctures for sample collection, for instance. In Argentina, a direct correlation was found between hair cortisol concentration and perceived stress, as well as between this hair concentration and the emotional exhaustion component of burnout, and it was identified that 12% of the nursing staff population studied presented burnout [19]. In Brazil, hair cortisol was obtained for the identification of stress, anxiety, and depression among 161 nursing professionals in a general hospital, and it was identified that 47.8% showed levels above normal; 23.8% presented moderate stress, 20.1% high stress, and 12.8% extremely high stress; 44.51% presented anxiety, and 24.39% presented depression [44]. Biomarkers were also identified in blood and urine samples by the studies included in this review. Thus, hematological markers, inflammatory markers, and oxidative damage in blood were obtained in a study carried out in Brazil [18], serum albumin, alpha 1, alpha 2, beta and gamma globulines, serum creatinine, and gamma-GT were obtained in a study carried out in Italy [20], as well as, still in this country, the number of lymphocytes and subpopulation of CD3+, CD4+, CD8+-CD57+, CD19+ and CD56+, cytotoxic activity and lymphoproliferative response from NK cells, serum concentrations of IL-1beta, IL-6, INF gamma and TNF alpha [22], genetic and immunotoxicological biomarkers, dosage of iron and serum glucose levels were identified in a study in Hungary [21]. In Taiwan, Republic of China, blood samples were obtained from 90 nurses for plasma copper, ferritin, interleukin (IL)-6, and alanine aminotransferase, considering that ferritin and IL-6 are important markers for the onset of depression [23]. In Belgium, volatile organic compounds (VOCs) and polycyclic aromatic hydrocarbons (PAHs) were identified in surgical smoke and the presence of their metabolites in the urine of surgeons and nursing professionals [24]. In blood and urine samples numerous markers can be obtained, such as: CRP - a protein that increases as part of the immune response to infection and is associated with general systemic or chronic inflammation [45,46,47]. Dehydroepiandrosterone Sulfate (DHEA), a common steroid in the body, one of the main mechanisms by which psychosocial stressors can affect individual health [48]. Sex Hormone-Binding Globulin (SHBG), a protein produced that is an endocrine biomarker, important for muscle maintenance [49].

Glucose, a biomarker of diabetes [47,50], Testosterone, an endocrine biomarker, a participant in maintaining muscle homeostasis [47,51]. High Density Lipoprotein (HDL) Cholesterol, which is associated with increased risks of Cardiovascular Disease [46,52]. Glycated Hemoglobin (HbA1c) or Glycosylated Hemoglobin (HbA1c) - which indicates the amount of hemoglobin (Hb) in the blood that is bound to glucose [46,47,50,53]. Hemoglobin (Hgb), which is responsible for transporting oxygen throughout the body [54]. Creatinine, a standard serological marker used to detect Acute Kidney Injury [55,56], Albumin - which represents 55% to 65% of total protein and maintains the osmotic blood pressure, preventing excessive flow of water into the tissues [46,47,57,58,59]. Total Protein, a nutritional biomarker [60], Rheumatoid Factor (RF), a common antibody type biomarker, which assists the immune system



in clearing excess antibodies from the bloodstream [61]. Sodium, a biomarker of nutritional and mineral balance; along with calcium and potassium, which are important for healthy muscles; calcium, bone, and nutritional biomarker, which are important for healthy muscles [62]. Vitamin D, a biomarker of bone, nutritional, and mineral balance [63], urea, renal biomarker of catabolic conditions [64], among others. Specifically, in the case of nursing professionals, a point that should be considered in the disease process is the perception and identification of risks to which professionals are exposed during their work. Such risks can be physical, chemical, biological, ergonomic, psychosocial, and accident-related [65]. However, they frequently are not perceived, recognized, and, consequently, acknowledged by the professionals, who then cannot adequately protect themselves against them and end up suffering physical and mental alterations. If the working conditions were more adequate in the nursing practice, if the wages were higher, and if the professionals received the appropriate Personal Protection Equipment, possibly there would be no need for professionals to have more than one job and, consequently, suffer alterations, both in their physical and mental health. Therefore, the use of biomarkers in studies with such professionals can assist in tracking diseases and in the diagnostic process. This tracking can then result in better prognoses and responses to treatments, as work activity can lead the person who performs it to become sick [66]. The professionals in this occupation are subject to inadequate working conditions, which favor health problems, which can be of a physical or psychological nature [67]. Aggravations are the damages to the physical, mental, and social integrity of individuals, which can be caused by diseases or hazardous circumstances, such as accidents, intoxications, drug abuse, and self-inflicted or hetero-inflicted injuries, often caused by the environments where people work [68]. The aggravations can generate eating disorders, sleep disorders, elimination disorders, fatigue, aggravations in the body systems, decreased alertness, stress, disorganization in the family environment, and neuroses, facts that often lead to work accidents, sickness, and leave for health treatment [69].

Although a certain tendency towards a gradual increase in studies with the use of biological markers involving nursing professionals has been observed, these studies are still restricted since they are expensive, dependent on equipment, equipped laboratories, specific kits and, sometimes, are longitudinal studies, with a greater demand of time for their execution. The use of biomarkers in research needs to be increased in order to better understand the relationship between the biological results obtained and the impacts of work on these professionals' health. Through scientific investigations using biological markers, it is more likely that more robust evidence can be obtained to demonstrate more clearly the stage of illness or the aspects that tend to lead professionals to become ill. Biomarkers are effective in the identification and treatment of several malignant pathologies, such as cancers [70]. Some conditions are essential for their use in occupational health, such as: How to explore their usefulness in regulation, especially in critical and emerging occupational health issues; having an adequate investment in the validation of biomarkers; the establishment of international guidelines for exposure levels, as well as a broad discussion in society regarding the ethical issues and social justice related to them [5,11]. For their use, in addition to clinical criteria, ethical discussions are necessary, as decisions regarding their use must be based on the best scientific, legal, and ethical evidence available [71]. In general, if biomarkers allow a great contribution to occupational health and safety, a more holistic approach will be needed to transfer them from the laboratory into professional practice, especially to be used as a tool in the management of occupational health.

Conclusion

The use of biomarkers for health assessment has been evidenced in studies with nursing professionals, presenting several investigative purposes. Therefore, they are a safe and effective trend for tracking and diagnosing diseases among professionals, and can promote earlier diagnosis and better prognosis for people affected by physical and mental alterations, providing the possibility of raising employers' and professionals' awareness to achieve better working and living conditions. In the present study, they assisted in the identification of health alterations in these professionals. Carrying out studies that use biological markers has the potential to improve the knowledge of nursing science, as it refers to biological information that indicates what happens, with greater precision, in the professionals' bodies. Through more robust and reliable results, it becomes possible to evidence more clearly the relationship between work and the illnesses experienced by professionals. If biomarkers have assisted in the identification of alterations in the health of nursing professionals and allowed a great contribution to occupational health and safety, a more holistic approach will be necessary to transfer them from the laboratory into professional practice, especially to be used as a tool in the management of occupational health. It is expected that such

evidence will demonstrate the need for changes in the workplace reality, as well as improvements in people's living and working conditions, thus mitigating the disease process and bringing benefits to these professionals' health.

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