Chapter

Impact of Occupational Stress and Its Associated Factors on Cognitive, Hormonal and Stress Responsive Protein in Mining Based Industrial Workers

Rajani G. Tumane, Shubhangi K. Pingle, Avinash S. Gaikwad and Beerappa Ravichandran

Abstract

Rapid globalization and technological advances have transformed the way of working. Occupational stress is psychological and physical condition that has potential to worsen a person's health in any workplace. Stress related productivity impairment were common in mining industries. Lack of skills, organizational issues, and a social support at workplace can all cause workers to experience stress. Therefore, hypothalamus-pituitary-adrenal (HPA) axis and sympathetic nervous system are activated as part of the body's physiological reaction. Hence chronic stress were linked to digestive, cardiovascular, atherosclerosis, and neurological issues. Numerous studies reported, several biochemical and pathophysiological factors were responsible for occupational, environmental, and workplace depression. This review chapter were included studied from PubMed, Google, book chapters, case reports, and other electronic databases, etc. Total (n = 104) articles were selected related to occupational stress and its impact on biochemical and pathophysiological were experienced in them. Workers who experienced occupational stress underwent pathophysiological changes that leads to changes in the stress hormones, sensitive stress protein and other significant variables. Finally, cortisol, stress hormones, PTH, HO-1, cytokines used as a panel of marker for stressful conditions evaluation in occupational settings. These findings, advice interventions that will be reduce, or eradicate some of these stressors in occupational settings.

Keywords: hormones, mining, neurological problems, occupational stress, pathophysiological changes, stress responsive protein

1. Introduction

World Health Organisation (WHO) reported that occupational stress is epidemic and characterised by the physical and mental toll that results from an imbalance between a people capability to manage with work-related stress and their objective

goals in occupational contexts [1, 2]. International Labour Organisation (ILO) reported, annually 2.34 million person die in occupational mishap and 25% deaths are attributable to dangerous and unhealthy occupational settings [3, 4]. Furthermore, non-fatal work-related disorders affected 160 million people. More than 200 million and 16 million workers exposed to various occupational toxic hazards and harmful exposures in factories respectively [5]. People are working harder than ever to improve society, jobs, education, health, and quality of life. Studies reported that the delicacy disorders brought via occupational related burnout in the US ranged from $500 to $1000 billion US dollar [6–8]. Other studies reported a favourable psychological and physiological condition in workers was maintained by factors like gender, age, and personality as well as self-perception, self-confidence, and stress tolerance [9, 10]. However, stress has a detrimental effect on employees' physical, emotional, and overall quality of life. These results into decreased output, job absenteeism, a loss of professional effectiveness, an increase in accident cases, a decline in morale, and interpersonal conflicts with subordinates [11–13]. Pilots, nurses, accountants, teachers, university employees, and managers have all been the subject of prior research that looked at occupational stress [14].

In occupational setting, miners and factory workers who were working in high stress condition and industrial demanding work environment. Exposure to hazardous substances in mining occupations affected biological system of human being. Several studies has been reported that metals, dust, noise, chemical factors, physical factors responsible for employees' psychological health problems leading to occupational burnout in humans but its cellular mechanism is still unclear in biochemical processes [15]. Further, hippocampus is the main part of the brain expresses the reaction of stressful stimuli which is responsible for involvement of distinct network reaction for occurrences of stress. Stress were also responsible for secretion of hormones including epinephrine and nor norepinephrine via by neuroendocrine mechanism. On the other hand, glucocorticoids were secreted by adrenal gland (hypothalamus pituitary adrenal). This leads to disturb oxidant and antioxidants levels responsible for development of oxidative stress in the human. Studies reported that the exposure to dust may cause various metabolic alterations in the biochemical, hormonal regulatory processes. These processes has potential to induce toxic effects in lung tissue of workers. Previous studies reported neurasthenia, anxiety disorder, and depression, occupational stress and psychological health problems due to occupational stress in different occupational groups [16, 17]. These findings necessitated further research on mine workers for evaluation of health risks due to occupational exposure to different pollutants. With this view, exposure markers, hemeoxygenase-1 (HO-1) and parathyroid hormones were targeted due to its special reference to occupational exposure to dust and development of job related stress in the workers. Studies reported that HO-1 was rate limiting enzyme which is induced in the lung during occupational stress condition. Other mechanism reported that parathyroid hormone (PTH) is involved in calcium regulation which is secreted by parathyroid gland and control by nervous endocrine system but overload of aluminium replaces calcium because of its same valence which suppression PTH levels in the Bauxite dust exposed workers in the occupational settings [18]. Limited attentions were noted to find out relationship between occupational stress and human individual factors were responsible for causing stress in the occupational setting workers. Studies on exposure biomarkers, aims to explore the occupational exposure to pollutants may be responsible for development of occupational stress through physiology, neurobiology, and stress proteins in the workers. It will also need to find out its impact on the quality of life of worker in the occupational settings.

2. Methodology

The MeSH (Medical Subject Headings) databases are the NLM controlled vocabulary thesaurus that were used for indexing articles such as occupational stress in workplaces, related diseases, factors affecting stress, consequences, occupational stress physiology and neurobiology, hormones involved in stress neurobiology and its mechanism of action, stress responsive parathyroid hormone (PTH) in occupational settings, stress responsive protein in occupational settings, oxidative stress markers in industrial based mining workers. Initial searches limited to materials available with complete abstracts and those available in the English language were included. Published articles were searched from numerous electronic databases including PubMed, Google, Cochrane library, free PMC article, koreamed, hinari publication, scopus indexed journal, virtual health library, audicus, NCBI databases, Indexing of Indian Medical Journals (INDMED), and PakMediNet—Medical Information Gateway of Pakistan etc. Systematic reviews, book chapters, review and research papers, and case studies pertaining to workplace stress in industrial settings were also included. Articles about stress in healthcare facilities, IT workplaces, academic institutions, and government institutions were omitted. Articles that only described the procedures or offered opinions or news were also disqualified. The review chapter were includes literature from 1986 to 2021 period (last 20 years) to study oxidative stress in mining based industrial subjects. A total of (n = 104) papers were chosen that discussed the effects of occupational stress on industrial employees' biochemistry and pathophysiology in stress conditions. According to the electronic database, very few published articles regarding stress protein expression in occupational stress conditions in mining based industrial workers from India were reported, This review chapter, discussed about occupational stress and its associated factors in workers which is continuously exposed to chemicals, dust, environmental pollutants, and hazardous toxicants had impact on their biochemical, pathophysiological, molecular, neurological, immunological, endocrine, and respiratory mechanisms alteration in them. These alteration may provide future insights regarding importance of occupational stress in them at workplace environment.

3. Factors affecting stress

Several industrial and organisational works related factors were found to be responsible for development of workplace stress. Bhatti et al. reported, 67% of the stress that employee's experiences were caused by both intra- and extra-organisational factors, with workload serving as the primary culprit [19]. Scientists had given more attention that one-third of the working population in affluent nations has moderate to severe levels of stress. Because of work environmental condition, its management and work consignment influences on employee physical and mental health. Similar research for newly industrialised nations also suggests that time constraints, unreasonable demands, role conflicts, poor ergonomics, job security, and relationships with customers are some of the most frequent sources of stress for workers in the financial services industry [20]. Furthermore, as a result of increased human involvement with computers, new stressors have emerged, including computer failures, computer slowdowns, and electronic performance monitoring etc. Many scientists reported that there are many moderate and non-moderated occupational stress factors that were contribute to occupational stress including working shifts,

sedentary, repetitive, lack of safety, monotonous work techniques, collaborative activities, uncontrollable jobs, physical elements (heat, noise, lighting, chemical elements like odour), interpersonal relationships of superiors at workplace, uncertainty, conflict, overwork, career development, reward, promotion, job security, and certainty of future employment [21–23]. Role of stress and key organisational outcomes have a complex link that can range from positive to negative results of various intensities responsible for affecting stress in humans at occupational settings [24].

4. Consequences of stress

A serious global problem is how occupational stress affects different occupational setting workers. A recent survey done by banker association found that 69% of banking and their staff were working in stressful condition and 50% reported psychological distress. Workers with low-back, hand, and arm issues as a result of linking musculoskeletal illnesses with the workplace, taking into account individuals, job tasks, and work environments, leave their positions and decrease the economic productivity of the country [25]. Workplace stress, way of life, and personal downtime have all been linked to the appearance of occupational stress in workers responsible for development of mental problems in them. Mining based industrial and factory workers were working relatively poor environment for longer period of time with no ventilation. Those workers belongs to below poverty line were responsible for varying degrees of job stress that affect workers quality of life [26]. Scientists have found that moderate and non-moderated occupational stress were responsible for hypertension, immune, nervous, and digestive impairment, depression, ischemic heart disease, psychological symptoms were responsible for reduction in the ability of employees to cope with their work [27–29]. Therefore, individuals may consume alcohol, reduction in appetite, and organisational performance [27–30]. Finally, individual, organisational-related components, behavioural disorders, family conflicts were might avoid people moving to do work, use drugs or drink excessively. Non moderated occupational stress was detrimental to professional workers' as well as disturb health and quality of life in job settings. Several studies were focused on workplace stress in medical staffs and banking employees who experienced higher levels of occupational stress had lower quality of life [29–31]. Therefore, occupational stress at workplace had described about unusual physiological, psychological, and behavioural reactions in workers due to occupational stress.

5. Occupational stress physiology and neurobiology

Technological advancements and rapid globalisation have changed the people how to work in ambient environmental conditions. In mining sectors, workers are constantly subjected to occupational and stress-related productivity degradation. The processing of work and coping with challenging situations needs the activation of intricate brain-body mechanisms. Neuroendocrine networks are involved in the different type mechanism and hippocampi expressed vide variety of stressful stimuli in the brain [32]. Homeostasis mechanism well maintained by the interactions among body organ systems and, its metabolic processes responsible for the release of free radicals including peroxynitrite radicals, hydrogen peroxides, superoxide anions, reactive oxygen species (ROS), and nitric oxide radicals in response to oxidative stress [33–36]. Studies well reported that stress condition were responsible for the

secretion of epinephrine, norepinephrine, and glucocorticoids hormones via neuroendocrine system in the brain. On the other hand, non-genomic, genomic, epigenetic processes, immune system stimulation, energy mobilisation, metabolic changes, and systemic inhibition were involved in the development of the oxidative stress in humans. Scientists placed more attention towards changes in cellular, synaptic and neural flexibility take place in combination with proinflammatory signals. Together, body-brain connection governs physiologic and behavioural changes were necessary for survival and sustainability [32, 37, 38]. Focusing on health hazardous problems and its impact on the workers in occupational settings disturbs mental and social health determinants in them. Studies reported that heavy metal fumes and dust exposure including, aluminium, lead, manganese, copper may get deposited into the brain. Excessive overload of heavy metals which cross the blood brain barrier and causes Alzheimer, Parkinson's schizophrenia and neurological diseases. The symptoms such as trembling slow motor movement, severe depression, anxiety, and loss of memory were well reported in them. Therefore, neuronal cells network mechanism was highly responsible for development of psychological problems due to oxidative stressors in them. However, neurotransmitter in the brain have neuronal connections which causes to release of proinflammatory cytokines directly responsible to disturb neurological mechanism and developed psychological issues in exposed workers [39, 40].

6. Hormones involved in stress neurobiology and its mechanism of action

Stress condition perturbs homeostasis of the human being gives large influences on human behavioural, endocrine system and cellular levels. Sympathetic (arousal) and parasympathetic (relaxation) nerve systems make up the autonomic nervous system. The automatic nervous system controls essential organs as well as visceral functions like respiration, digestion, circulation, and temperature regulation. In stress condition, the hypothalamus carries several distinct tasks which secretes arginine vasopressin, antidiuretic hormone, stimulates the hypothalamus gland. Scantamburlo et al. [41] claim that anterior pituitary gland results into production of ACTH in response to corticotropin releasing hormone (CRH) [40, 42]. Further, adrenal cortex (outer part) is stimulated by ACTH to release corticoids (glucocorticoids and mineralocorticoids). The main function of glucocorticoids is to release energy by conversion of glycogen into glucose and breakdown of fats into fatty acids and glycerol, which is needed to combat the negative consequences of a stressor [41, 43–45]. In addition, corticoids which inhibit the immune system, reduce hunger, aggravate gastrointestinal irritation, and associated feeling of depression and loss of control in stress conditions. On the other hand, aldosterone, a mineralocorticoid, encourages the retention of Na^+ and the removal of K^+. These reaction results into high blood pressure, heart rate, dilated pupils, constricted arteries to non-working muscles, and force to cardiac contraction. In addition, ADH known to maintain the blood pressure during stress when the body's equilibration is upset. Regulating fluid loss through the urinary system is the primary function of vasopressin (ADH), which is produced by the hypothalamus and released by the posterior pituitary. Further, the second significant alteration occurs during release of energy and distributions of energy to different organ system were needed. In addition, growth hormone (GH) and thyroid hormones played important role in stress condition. Due to stress condition, GH and thyroid hormones increased psychological stimuli in humans [46]. The thyroid gland secretes thyroxin and triiodothyronine which plays very important role

in the management of stress in the human body. Thyroid hormones' primary purpose is to boost basal metabolic rate, and raises heart rate and increase in the levels of catecholamines in stress situation. Despite, stress hormones, serotonin and melatonin are linked to mood. Depression is well connected with neurological problem and its reduction in stress in occupational setting is well reported [47–50].

Depression is well connected with neurological problem and its reduction in stress hormones in occupational setting are well reported [47–50].

7. Oxidative stress markers in mining workers

The oxidants and antioxidants imbalance causes oxidative stress, which disrupts redox signalling and physiological function of the cell in humans. OS executed redox signalling-induced alterations, which might alter transcriptional activity, kinases networks, and apoptosis [51–55]. Studies reported that s-nitrosation, disulfide linkages, s-nitrosylation, S-glutathionylation, and sulfenylation proteins undergo discrete, reversible, and site specific alterations of cysteine residues to create redox signalling [56–58]. Exploring their potential clinical applications, nevertheless, continues to spark growing interest. Studies on oxidative stress markers in a variety of human diseases are being reported in published manuscripts. Thus, lot of focus on the analytical challenges needs to validate oxidative stress indicators in stressful condition [59, 60]. Although numerous indicators and techniques are employed but many of them lack strong correlations, fail to accurately reflect oxidative stress, and lack of specificity in occupational diseases in dust exposed workers. Recent studies reported that black lung in coal workers is caused due to bioavailable iron (BAI) present in the coal dust. The iron occurs in the coal dust reacts with the oxygen and oxygen peroxide and forms ROS. The ROS acts as a mediators which stimulate the activation of alveolar macrophage, immune cells and tend to release cytokines. The lung is a vulnerable organ to exogenous ROS because of its anatomy, function, and location where development of pulmonary diseases due to endogenous ROS. The lower respiratory tract becomes clogged with inflammatory mediators and activated phagocytotic cells, which produces ROS to protect respiratory system from environmental pollutant in the occupational settings. However, deposition of dust particle in alveolar macrophages activates the lung oxidative stress mechanism through the release of pro-inflammatory marker by ROS which damages DNA, protein, lipids etc. which causing lung disease in exposed workers. Studies confirmed that OS and the pro-inflammatory cytokines were involved in the progression of fibrotic lung disease in coal dust-induced pneumoconiosis, and progressive massive fibrosis (PMF) [61–64]. Recently, oxidative stress markers were reported in developed in-vitro model of alveolar epithelial (A549) and monocytic lung (U937) cell line for pneumoconiosis along with antioxidant enzymes. Oxidative stress parameter in the alveolar macrophage and lung epithelial cells exposed to coal dust results in the significant elevation in the oxidative stress markers NADPH, MPO, MDA and PC & reduction of antioxidant content (i.e. SOD, CAT and GSH). Results indicated that imbalance in the generation of ROS species and antioxidant enzyme could be one of the key payers to initiate the inflammation causing chronic tissue damage and fibrosis in the lung tissue. Coal exposure played a key role in the aetiology of asthma and chronic bronchitis (CB) [65–67]. By looking at oxidation target products, such as malonoaldehyde (end product of Lipid peroxidation), DNA damage, protein carbonyls, 8-isoprostane, DNA oxidation, and other oxidative stress markers generated by ROS can be evaluated either directly or indirectly. They can be used to evaluate

oxidative stress in humans since they are molecules whose structures have been altered by ROS. Antioxidant molecules including glutathione, protein thiols, and enzymatic antioxidant activity are further biomarkers of oxidative stress and key players in the body's antioxidant defence mechanism and a subject of extensive research [68, 69]. Finally, antioxidant enzymes, oxidants and proinflammatory cytokine markers may be used for OS in occupationally developed diseases in exposed workers.

8. Stress responsive parathyroid hormone (PH) in occupational settings

Corticosterone (CORT) is stress regulating hormone in human and its reduction in cortisol levels causes low blood pressure, fatigue, weakness in stress condition. Addison's disease, damage adrenal gland, neurological, immunological and metabolic effects were reported in stress condition. Importantly, CORT is responsible to reduce calcium absorption levels and reabsorption from intestine, kidney by increasing the secretion of PH hormones [50, 70, 71]. Parathyroid hormone involved in the calcium regulation which is secreted by parathyroid gland and control via hypothalamus axis. The main mechanism of action of PTH that exerts its effects on kidney, bone and intestine via tubular reabsorbtion and absorption of calcium. Scientists reported that interconnection between parathyroid gland and CORT during first trimers were maintained via differentiation of bone cells and chondrocytes [72]. Recently, PTH suppression in occupationally Bauxite dust exposed workers were reported at the time smelting, mining operations, and beneficiation of Bauxite but its impact in response to stress were less approached by scientists [73, 74]. Therefore, experimental studies reported that aluminium overload supressed PTH levels but still not yet confirmed and indistinguishable that whether Al involved in decline in synthesis/release of PTH because aluminium toxicity effect on bone metabolism and changes in calcium and phosphorus can be modulated by PTH [75, 76]. Earlier reported that Aluminium suppresses PTH by increasing calcium levels and directly affected PTH synthesis this suggested that direct approach is frequent and important as compared to indirect PTH inhibition. Therefore, agreed with serious effects of aluminium in bones that is multi factorial which alters mineralisation, cellular activity of bone cells and leads to cell death because of alteration in cell metabolism [77–80]. The interconnection of aluminium, Calcium, and PTH were well reported but in context to occupational Bauxite dust exposed workers studies not yet reported. In-vitro and in-vivo studies showed that both indirect and direct methods helped evaluation of effect of Al on parathyroid function. Decreased level of PTH with increased Al levels were observed in the occupationally dust exposed bauxite workers. Further, significant negative correlation were observed between PTH and blood aluminium levels and inverse correlation were noted between PTH and calcium. Other studies reported that Al overload decreased PTH and calcium in circulating system [80, 81]. From this studies were suggested that direct and indirect PTH regulation mechanism and Al interferes in PTH secretion/release rather than its synthesis.

9. Stress responsive protein in occupational settings

Heme oxygenase-1 (HO-1) has been identified in many different cell types from lower to higher organisms to tolerate the different forms of stress. Environmental influence alters the pattern of cellular protein expression, performs physiological

activities by acting as a molecular chaperon [82]. Anti-inflammatory actions of HO-1 (rate limiting enzyme) in biochemical pathways are may be due to breakdown of the pro-oxidant heme by own, signal effects of carbon monoxide (CO), the antioxidant biliverdin/bilirubin, and the sequestration of free iron by ferritin in human. Stress responsive HO-1 protein has ability to inhibit inflammation and provide cytoprotection that can be attributed through by-product of HO-1. Heme oxygenase another form of protein, HO-2 were present in neurones and astrocytes, but HO-1 generally worked as inducible form in cell types of central nervous system and by product of HO-1 performs similar work [83, 84]. Numerous stimuli can induce HO-1 gene expression, including oxidative stress and Aβ peptides [85–88]. Induction of HO-1 occurs due to inflammatory processes insults of the cells by environmental factors and the activation of an oxidative stress generated by nuclear factor erythroid 2-related factor-2 (Nrf2), Interleukin-1 (IL-1), and other inflammatory markers. Induction of HO-1 were regulated through Nrf2 contain transcription factor BTB and CNC homology 1 (Bach1) competes with Nrf2 and represses transcription factors [89, 91]. The Nrf2 present in the cytoplasm which interacted with Kelch-like ECH associating protein 1 (Keap1). Keap1 which regulated Nrf2 activity and behave as a sensor for oxidative and electrophilic stresses, degraded by the ubiquitin proteasome pathway. Finally, Nrf2 slightly accumulated in the nucleus and inhibited transcription of the HO-1 gene. Thus, Nrf2-Keap1 complex system played as role in defence mechanism in human [92–95].

In occupational settings, high levels of HO-1 were reported due to bauxite dust exposure and responsible for catabolism of heme in aluminium exposed workers [96]. High levels of Al reported in bauxite exposed workers were assorted and its cellular mechanism fails to appear in published article. Other studies reported that decrease in the level of haemoglobin and high levels of HO-1 in Bauxite dust exposure group which may be due to increased catabolism of heme and generation of ROS and OS in them [97]. Previous study reported that HO-1 deficient and heavy metal exposure at cellular level were more prone to cytotoxicity injury. The functional role of HO-1 induction in OS is not well established in the occupational settings. HO-1 exerts protective role as neurodegenerative, cardiovascular, cancer, metabolic, iron metabolism disorders and various inflammatory diseases in human after oxidative injury [98]. Scientist gave more attention towards role of Ho-1 in silicotic patients, respiratory diseases, and asthma in sub mucosal macrophages and airway epithelium which helps to defend against the insults in lungs in the occupational settings [99–104]. However, induction and molecular regulation HO-1 acts as a anti-inflammatory, antioxidative and antiapoptotic and in response to oxidative stress.

10. Conclusion

The current chapter, assessed the trends in global research on stress at occupational settings. For the enrichment of life in the mining industries and other workplace areas, workers were continuously working in stressful job environments for the betterment of life in mining industries and other workplace areas. In stressful environment, subjects were exposed to chemicals, dust, environmental pollutants and hazardous toxicants ultimately alters biochemical, pathophysiological changes, molecular, neurological, immunological, endocrine, and respiratory mechanisms alteration in them. The deposition of dangerous pollutants in brain, kidney, lungs and

other part of human system and results into the occurrences of several serious health hazards and diseases in exposed workers. Its impact reported neurological, oxidant and antioxidant level changes, respiratory illnesses, Alzheimer's, Parkinson's, infectious issues, and immunological disturbances in exposed workers of occupational settings. This study's findings were significant for understand the epidemiological issues in occupational settings, which has drawn increased attention. According to reports, high income, control job categories that were linked to lower job stress. However, a psychological problem, which has a positive predictive impact on quality of life, is a mediator in the association between occupational stress and quality of life. Growing health concerns have raised awareness of the importance of researching difficult technologies that have not been used in India yet. Research suggests that cortisol, epinephrine, non-epinephrine, PTH, HO-1, antioxidant enzymes, proinflammatory cytokines, prooxidant levels were helpful as a panel of marker for evaluation of significant stressful conditions in exposed subjects. The growing health concern has been an increasing awareness about the need to do study on occupational stress factors yet not implemented fully in India. Study findings could help to advise interventions that reduce, minimise or eradicate some of these stressors in occupational settings.

Author details

Rajani G. Tumane, Shubhangi K. Pingle*, Avinash S. Gaikwad
and Beerappa Ravichandran
ICMR-Regional Occupational Health Centre (S), NIOH, Bengaluru, Karnataka, India

*Address all correspondence to: pingle.shubhangi@gmail.com

References

[1] van der Meij L, Gubbels N, Schaveling J, Almela M, van Vugt M. Hair cortisol and work stress: Importance of workload and stress model (JDCS or ERI). Psychoneuroendocrinology. 2018;**89**:78-85

[2] Qian LJ. Strengthen the study of occupational stress in China. Chin. J. Occup. Dis. Lab. Health. 2003;**21**:1-2 (In Chinese)

[3] Lu Y, Zhang Z, Yan H, Rui B, Liu J. Effects of occupational hazards on job stress and mental health of factory workers and miners: A propensity score analysis. BioMed Research International. 2020;**2020**:1754897. DOI: 10.1155/2020/1754897

[4] Chartres N, Bero LA, Norris SL. A review of methods used for hazard identification and risk assessment of environmental hazards. Environment International. 2019;**123**:231-239

[5] Shafiei M, Ghasemian A, Eslami M, Nojoomi F, Rajabi-Vardanjani H. Risk factors and control strategies for silicotuberculosis as an occupational disease. New Microbes and New Infections. 2018;**27**:75-77

[6] Ivanka S. Structural changes of the brain in relation to occupational stress. Cerebral Cortex. 2013;**12**:321-324. [Google Scholar]

[7] Matić M, Jovanović J, Jovanović J, Mačvanin N. Effects of occupational stress on working ability of patients suffering from arterial hypertension. Medicinski Pregled. 2013;**66**:497-501. DOI: 10.2298/MPNS1312497M

[8] Cooper CL. Occupational stress among international interpreters. Occupational Medicine. 1993;**25**:889-895. DOI:10.1097/00043764-198312000-00012

[9] Zhu TJ. Investigation and Study on occupational tasks of dust-exposed workers in coal mines. Chinese Journal of Pharmaceutical Analysis. 2012;**8**:1007-1011 (In Chinese)

[10] Bhatti N, Shar AH, Shaikh FM, Nazar MS. Causes of stress in organization, a case study of Sukkur. International Journal of Business and Management. 2010;**5**(11):3-14

[11] Zhang Q. Occupational injury occurrence and related risk factors among Chinese migrant workers. Procedia Engineering. 2012;**43**:76-81

[12] Choi SD, Guo L, Kim J, Xiong S. Comparison of fatal occupational injuries in construction industry in the United States, South Korea, and China. International Journal of Industrial Ergonomics. 2019;**71**:64-74

[13] Cullen MR, Chmiack MG, Rosenstock L. Occupational medicine. New England Journal of Medicine. 1990;**322**:594-601. DOI: 10.1056/NEJM199003013220905

[14] Mani KP, Sritharan, Gayatri R. Impact of occupational stress on quality work life among railway station masters of Trichy division. Bonfring International Journal of Industrial Engineering and Management Science. 2014;**4**:165-169. DOI: 10.9756/BIJIEMS.6129

[15] Parent-Thirion, Biletta I, Cabrita J, Llave VO, Vermeylen G, Ilczynska A. 6th European Working Conditions Survey: Overview Report. Luxembourg: Publications Office of the European Union; 2017

[16] Rausch SM, Auerbach SM, Gramling SE. Gender and ethnic differences in stress reduction reactivity and recovery. Sex Roles. 2008;**59**:726-737. DOI: 10.1007/s11199-008-9460-0

[17] Quick JC, Tetrick LE. Handbook of Occupational Health Psychology. Washington, DC, USA: American Psychological Association; 2003. pp. 97-119

[18] Shultz KS, Wang M, Crimmins EM, Fisher GG. Age differences in the demand-control model of work stress: An examination of data from 15 European Countries. Journal of Applied Gerontology. 2010;**29**:21-47. DOI: 10.1177/0733464809334286

[19] Anderson ES, Coffey SB, Byerly TR. Formal organizational initiatives and informal workplace practices: Links to work-family conflict and job-related outcomes. Journal of Management. 2002;**28**(6):787-810

[20] Chou LP, Li CY, Hu SC. Job stress and burnout in hospital employees: Comparisons of different medical professions in a regional hospital in Taiwan. BMJ Open. 2014;**4**:e004185. DOI: 10.1136/bmjopen-2013-004185

[21] Dewa CS, Thompson AH, Jacobs P. Relationships between job stress and worker perceived responsibilities and job characteristics. International Journal of Occupational and Environmental Medicine. 2011;**2**:37-46. [Google Scholar]

[22] Härmä M. Workhours in relation to work stress, recovery and health. Scandinavian Journal of Work, Environment & Health. 2006;**32**:502-514. DOI: 10.5271/sjweh.1055

[23] Gangster, Logan. Effects of stress on workers. Indian Journal of Industrial Relations. 2005;**38**(5):280-287

[24] Kumar Das P. Work Related Stress among Coal Mine workers: A study on select coal mines of Dhanbad & Jharia regions. International Journal on Arts, Management and Humanities. 2018;**7**(1):56-70

[25] Malamardi SN, Kamath R, Tiwari R, Nair BVS, Chandrasekaran V, Phadnis S. Occupational stress and health-related quality of life among public sector bank employees: A cross-sectional study in mysore, Karnataka, India. Indian Journal of Occupational and Environmental Medicine. 2015;**19**:134-137

[26] Liu L, Wu H, Yang YL. The mediating effect of psychological capital of underground miners on the relationship between occupational stress and anxiety symptoms. China Health Statistics. 2016;**33**:209-211 214

[27] Deguchi Y, Inoue K. Relationships between occupational stress and depressive symptoms among prison officers in Japan. Osaka City Medical. 2013;**59**:91-98. [Google Scholar]

[28] Rutter DR, Loregrove MJ. Occupation Stress and its predictors in radiographer. Radiography. 2008;**14**:138-143. DOI: 10.1016/j.radi.2006.09.008

[29] Morita N, Wada I. Job stress and mental health of child counselling office worker. Journal of Occupational Health. 2007;**49**:125-133. DOI: 10.1539/joh.49.125

[30] Wang RG, Zhao XB. Analysis of occupational stress among medical workers. Occupational Health Injections. 2002;**17**:181-183. [Google Scholar]

[31] Zhang Y, Liang DH, Shi XZ, Geng QY, Liu Y. Survey on occupational stress and quality of life of medical staff in Shenyang. Occupational and Environmental Medicine. 2012;**29**:572-575

[32] Azimbagirad M, Junior LO. Tsallis generalized entropy for Gaussian mixture model parameter estimation on brain segmentation application. Neuroscience Informatics. 2021;**1**(1-2):100002

[33] Krumova K, Cosa G. Chapter 1: Overview of reactive oxygen species. In: Singlet Oxygen: Applications in Biosciences and Nanosciences. Vol. 1. Royal Society of Chemistry. 2016. pp. 1-21. DOI: 10.1039/9781782622208-00001

[34] Mittal M, Siddiqui MR, Tran K, Reddy SP, Malik AB. Reactive oxygen species in inflammation and tissue injury. Antioxidants & Redox Signaling. 2014;**20**(7):1126-1167. DOI: 10.1089/ars.2012.5149. Epub 2013 Oct 22

[35] Di Meo S, Reed TT, Venditti P, Victor VM. Role of ROS and RNS sources in physiological and pathological conditions. Oxidative Medicine and Cellular Longevity. 2016;**2016**:1245049. DOI: 10.1155/2016/1245049. Epub 2016 Jul 12

[36] Smith SM, Vale WW. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues in Clinical Neuroscience. 2006;**8**(4):383-395. DOI: 10.31887/DCNS.2006.8.4/ssmith

[37] Becks MJ, Manniesing R, Vister J, Pegge SA, Steens SC, van Dijk EJ, et al. Brain CT perfusion improves intracranial vessel occlusion detection on CT angiography. Neuroradiology Journal. 2019;**46**(2):124-129

[38] Tchofo PJ, Balériaux D. Brain 1H-MR spectroscopy in clinical neuroimaging at 3T. Journal of Neuroradiology. 2009;**36**(1):24-40

[39] Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. JAMA. 2007;**298**(14):1685-1687

[40] Dayas CV, Buller KM, Crane JW, Xu Y, Day TA. Stressor categorization: Acute physical and psychological stressors elicit distinctive recruitment patterns in the amygdala and in medullary noradrenergic cell groups. The European Journal of Neuroscience. 2001;**14**(7):1143-1152

[41] Scantamburlo G, Ansseau M, Legros JJ. Implication de la neurohypophysedans le stress psychique [Role of the neurohypophysis in psychological stress]. Encephale. 2001;**27**(3):245-259. French

[42] Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, et al. Regulation of the hypothalamic-pituitary-adrenocortical stress response. Comprehensive Physiology. 2016;**6**(2):603-621. DOI: 10.1002/cphy.c150015

[43] Sharma DK. Physiology of stress and its management. Journal of Medicine Study & Research. 2018;**1**:001

[44] Hinson AV, Aguèmon B, Adjobimey M, Damien GB, Ouili I, Mikponhoue R, et al. Prevalence and associated factors of occupational stress in the mining sector: The case study of the Youga Mine at Zabre in Burkina Faso. Occupational Diseases and Environmental Medicine. 2021;**9**:185-198

[45] Selye H. The Stress of Life. New York: McGraw-Hill; 1956

[46] Ranabir S, Reetu K. Stress and hormones. Indian Journal of Endocrinology. 2011;**15**(1):18-22. DOI: 10.4103/2230-8210.77573

[47] Himi T, Takano K, Yamamoto M, Naishiro Y, Takahashi H. A novel concept of Mikulicz's disease as IgG4-related disease. Auris Nasus Larynx. 2012;**39**(1):9-17. DOI: 10.1016/j.anl.2011.01.023. Epub 2011 May 14

[48] Munck A, Naray-Fejes-Toth A. Glucocorticoid action. In: DeGroot LJ, editor. Endocrinology. 3rd ed. Philadelphia: W B Saunders; 1995

[49] Mayer EA. The neurobiology of stress and gastrointestinal disease. Gut. 2000;**47**(6):861-869. DOI: 10.1136/gut.47.6.861

[50] Goncharova ND. Stress responsiveness of the hypothalamic-pituitary-adrenal axis: Age-related features of the vasopressinergic regulation. Frontiers in Endocrinology. 2013;**4**:26. DOI: 10.3389/fendo.2013.00026

[51] Sies H. Biochemistry of oxidative stress. Angewandte Chemie. 1986;**25**: 1058-1071

[52] Sies H. Oxidative stress: A concept in redox biology and medicine. Redox Biology. 2015;**4**:180-183

[53] Foster DB, Van Eyk JE, Marbán E, O'Rourke B. Redox signalling and protein phosphorylation in mitochondria: Progress and prospects. Journal of Bioenergetics and Biomembranes. 2009;**41**:159-168

[54] Frijhoff J, Dagnell M, Godfrey R, Ostman A. Regulation of protein tyrosine phosphatase oxidation in cell adhesion and migration. Antioxidants & Redox Signaling. 2014;**20**:1994-2010

[55] Hool LC, Corry B. Redox control of calcium channels: From mechanisms to therapeutic opportunities. Antioxidants & Redox Signaling. 2007;**9**:409-435

[56] Vita JA, Brennan M-L, Gokce N, Mann SA, Goormastic M, Shishehbor MH, et al. Serum myeloperoxidase levels independently predict endothelial dysfunction in humans. Circulation. 2004;**110**:1134-1139

[57] Janssen-Heininger YMW, Mossman BT, Heintz NH, Forman HJ, Kalyanaraman B, Finkel T, et al. Redox-based regulation of signal transduction: principles, pitfalls, and promises. Free Radical Biology and Medicine. 2008;**45**:1-17

[58] Jones DP, Go Y-M. Mapping the cysteine proteome: Analysis of redox-sensing thiols. Current Opinion in Chemical Biology. 2011;**15**:103-112

[59] Dalle-Donne I, Rossi R, Colombo R, Giustarini D, Milzani A. Biomarkers of oxidative damage in human disease. Clinical Chemistry. 2006;**52**:601-623

[60] Leiper J, Nandi M. The therapeutic potential of targeting endogenous inhibitors of nitric oxide synthesis. Nature Reviews. Drug Discovery. 2011;**10**:277-291

[61] Tkaczyk J, Vizek M. Oxidative stress in the lung tissue—Sources of reactive oxygen species and antioxidant defence. Prague Medical Report. 2007;**108**:105-114

[62] Bargagli E, Olivieri C, Bennett D, Prasse A, Muller-Quernheim J, Rottoli P. Oxidative stress in the pathogenesis of diffuse lung diseases: A review. Respiratory Medicine. 2009;**103**:1245-1256. DOI: 10.1016/j.rmed.2009.04.014

[63] Villegas L, Stidham T, Nozik-Grayck E. Oxidative stress and therapeutic development in lung diseases. Journal of Pulmonary & Respiratory Medicine. 2014;**4**:194. DOI: 10.4172/2161-105X.1000194

[64] Zosky GR, Hoy RF, Silverstone EJ, Brims FJ, Miles S, Johnson AR, et al. Coal workers' pneumoconiosis: An Australian perspective. The Medical Journal of Australia. 2016;**204**(11):414-418

[65] Fujimura N. Pathology and pathophysiology of pneumoconiosis. Current Opinion in Pulmonary Medicine. 2000;**6**(2):140-144

[66] Huang C et al. Role of bioavailable iron in coal dust-induced activation of activator protein-1 and nuclear factor of activated T cells: Difference between Pennsylvania and Utah Coal Dusts. American Journal of Respiratory Cell and Molecular Biology. 2002;**27**(5):568-574

[67] Zhang Q, Dai J, Ali A, Chen L, Huang X. Roles of bioavailable iron and calcium in coal dust-induced oxidative stress: Possible implications in coal workers' lung disease. Free Radical Research. 2002;**36**(3):285-294

[68] Nagaraj Priyadarshini MD. Systemic oxidative stress and antioxidant status in chronic bronchitis patients. Journal of Scientific and Innovative Research. 2014;**3**:234-238

[69] Zinellu E, Zinellu A, Fois AG, Fois SS, Piras B, Carru C, et al. Reliability and usefulness of different biomarkers of oxidative stress in chronic obstructive pulmonary disease. Oxidative Medicine and Cellular Longevity. 2020;**2020**:1-12. DOI: 10.1155/2020/4982324

[70] Chrousos G, Pavlaki AN, Magiakou MA. Glucocorticoid therapy and adrenal suppression. In: De Groot LJ, Chrousos G, Dungan K, Feingold KR, Grossman A, Hershman JM, et al., editors. Endotext [Internet]. South Dartmouth (MA): 2000. MDText.com. [Google Scholar]

[71] Zhang H, Zhou Z, Luo J, Hou J. Effects of corticosterone on the metabolic activity of cultured chicken chondrocytes. BMC Veterinary Research. 2015;**11**:86. DOI: 10.1186/s12917-015-0398-5

[72] Poole KE, Reeve J. Parathyroid hormone—A bone anabolic and catabolic agent. Current Opinion in Pharmacology. 2005;**5**(6):612-617. DOI: 10.1016/j.coph.2005.07.004

[73] Nieboer E, Gibson BL, Oxman AD, et al. Health effects of aluminum: A critical review with emphasis on aluminum in drinking water. Environmental Reviews. 1995;**3**:29-81

[74] CannataAndia JB. Aluminium toxicity: Its relationship with bone and iron metabolism. Nephrology Dialysis Transplantation. 1996;**11**(Suppl 3):69-73. DOI:10.1093/ndt/11.supp3.69. PMID: 8840317

[75] Carmen DC, Jose LF, Barreto S, et al. Effect on aluminium load on parathyroid hormone synthesis. Nephrology Dialysis Transplantation. 2001;**16**(4):742-745. DOI: 10.1093/ndt/16.4.742. PMID: 11274267

[76] Jeffery EH, Abreo K, Burgess E, et al. Systemic aluminum toxicity: Effects on bone, hematopoietic tissue, and kidney. Journal of Toxicology and Environmental Health. 1996;**48**(6):649-665

[77] Cournot WG, Plachot JJ, Bordeau A. Effect of aluminium on bone and cell localization. Kidney International. 1986;**37**:-40

[78] Sua'rez-Ferna'ndez MB, Soldado AB, Sanz-Medel A, et al. Aluminum-induced degeneration ofastrocytes occurs via apoptosis and results in neuronal death. Brain Research. 1999;**835**(2):125-136. DOI: 10.1016/s0006-8993(99)01536-x

[79] Pan JW, Zhu MY, Chen H. Aluminum-induced cell death in root-tip cells of barley. Environmental and Experimental Botany. 2001;**46**(1):71-79

[80] Aremu DA, Meshitsuka S. Accumulation of aluminum by primary cultured astrocytes from aluminum amino acid complex and its apoptotic effect. Brain Research. 2005;**1031**(2):284-296

[81] Jorde R, Saleh F, Figenschau Y, Kamycheva E, Haug E, Sundsfjord J. Serum parathyroid hormone (PTH) levels in smokers and non-smokers. The fifth Tromsø study. European Journal of Endocrinology. 2005;**152**:39-45

[82] Schipper HM. Heme oxygenase expression in human central nervous system disorders. Free Radical Biology and Medicine. 2004;**37**:1995-2011

[83] Kim HP, Ryter SW, Choi AM. CO as a cellular signaling molecule. Annual Review of Pharmacology and Toxicology. 2006;**46**:411-449

[84] Ryter SW, Alam J, Choi AM. Heme oxygenase-1/carbon monoxide: From basic science to therapeutic applications. Physiological Reviews. 2006;**86**:583-650

[85] Wu L, Wang R. Carbon monoxide: endogenous production, physiological functions, and pharmacological applications. Pharmacological Reviews. 2005;**57**:585-630

[86] Dennery PA. Regulation and role of heme oxygenase in oxidative injury. Current Topics in Cellular Regulation. 2000;**36**:181-199

[87] Dwyer BE, Nishimura RN, Lu SY. Differential expression of heme oxygenase-1 in cultured cortical neurons and astrocytes determined by the aid of a new heme oxygenase antibody. Response to oxidative stress. Brain Research. Molecular Brain Research. 1995;**30**:37-47

[88] Pappolla MA, Chyan YJ, Omar RA, Hsiao K, Perry G, Smith MA, et al. Evidence of oxidative stress and in vivo neurotoxicity of beta-amyloid in a transgenic mouse model of Alzheimer's disease: A chronic oxidative paradigm for testing antioxidant therapies in vivo. The American Journal of Pathology. 1998;**152**:871-877

[89] Jaiswal AK. Nrf2 signaling in coordinated activation of antioxidant gene expression. Free Radical Biology & Medicine. 2004;**36**:1199-1207. DOI: 10.1016/j.freeradbiomed.2004.02.074

[90] Ogawa K, Sun J, Taketani S, Nakajima O, Nishitani C, Sassa S, et al. Heme mediates derepression of Maf recognition element through direct binding to transcription repressor Bach1. The EMBO Journal. 2001;**20**:2835-2843. DOI: 10.1093/emboj/20.11.2835

[91] Tian W, Rojo de la Vega M, Schmidlin CJ, Ooi A, Zhang DD. Kelch-like ECH-associated protein 1 (KEAP1) differentially regulates nuclear factor erythroid-2-related factors 1 and 2 (NRF1 and NRF2). The Journal of Biological Chemistry. 2018;**293**(6):2029-2040. DOI: 10.1074/jbc.RA117.000428. Epub 2017 Dec 18

[92] Igarashi K, Sun J. The heme-Bach1 pathway in the regulation of oxidative stress response and erythroid differentiation. Antioxidants & Redox Signaling. 2006;**8**:107-118

[93] Morse D, Lin L, Choi AM, Ryter SW. Heme oxygenase-1, a critical arbitrator of cell death pathways in lung injury and disease. Free Radical Biology and Medicine. 2009;**47**:1-12. [Google Scholar]

[94] Jang S, Piao S, Cha YN, Kim C. Taurine chloramine activates Nrf2, increases HO-1 expression and protects cells from death caused by hydrogen peroxide. Journal of Clinical Biochemistry and Nutrition. 2009;**45**:37-43. [Google Scholar]

[95] Cho HY, Reddy SP, Kleeberger SR. Nrf2 defends the lung from oxidative stress. Antioxidants & Redox Signaling. 2006;**8**:76-87

[96] Danielle M, Augustine MKC. Heme Oxygenase-1 from Bench to Bedside. American Journal of

Respiratory and Critical Care Medicine. 2005;**172**:660-670

[97] Murakami T, Watanabe M, Tezuka M. Induction of heme oxygenase-1 by aluminium and lack of effects of antioxydants. Journal of Health Science. 1999;**45**:33

[98] Dunn LL, Midwinter RG, Ni J, Hamid HA, Parish CR, Stocker R. New insights into intracellular locations and functions of heme oxygenase-1. Antioxidants & Redox Signaling. 2014;**20**:1723-1742. DOI: 10.1089/ars.2013.5675

[99] Lim S, Groneberg D, Fischer A. Expression of heme oxygenase isoenzymes 1 and 2 in normal and asthmatic airways effect of inhaled corticosteroids. American Journal of Respiratory and Critical Care Medicine. 2000;**162**:1912-1918

[100] Sato T, Takeno M, Honma K, et al. Heme-oxygenase-1, a potential biomarker of chronic silicosis, attenuates silica-induced lung injury. American Journal of Respiratory and Critical Care Medicine. 2006;**174**:906-914

[101] Fredenburgh LE, Perrella MA, Mitsialis SA. The role of heme oxygenase-1 in pulmonary disease. American Journal of Respiratory Cell and Molecular Biology. 2007;**36**:158-165

[102] Wagner M, Hermanns I, Bittinger F. Induction of stress proteins in human endothelial cells by heavy metal ions and heat shock. The American Physiological Society. 1999;**277**(5):L1026-L1033

[103] Yachie A. Heme oxygenase-1 deficiency and oxidative stress: A review of 9 independent human cases and animal models. International Journal of Molecular Sciences. 2021;**22**(4):1514. DOI: 10.3390/ijms22041514

[104] Hettiarachchi N, Dallas M, Al-Owais M, Griffiths H, Hooper N, Scragg J, et al. Heme oxygenase-1 protects against Alzheimer's amyloid-β1-42-induced toxicity via carbon monoxide production. Cell Death & Disease. 2014;**5**(e1569). DOI: 10.1038/cddis.2014.529