# Examination of Salivary Cortisol as a Biomonitoring of Work-Related Stress

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**ABSTRACT**

**Introduction:** Stress is a condition that must bepaid attention to by workers and employers, 87% of the workers from Europe claimed that they suffered from stress in the workplace. In 2015 around 28% of the workers reported suffering from work-related stress, with 33% clinical manifestations of fatigue, 19% sleep disturbances and 18% anxiety. Impacts that can affect workers can be absenteeism, presenteeism, etc. This study aims to investigate salivary cortisol examination to examine work-related stress using the evidence-based case report method. **Methods:** A literature review was conducted on November 23, 2020 through searches on the PubMed, Cochrane, and Google Scholar databases to find all published observational studies evaluating the relationship between salivary cortisol and work-related stress. **Results:** After screening using inclusion criteria and reducing the duplication of articles, 5 articles were obtained. **Conclusion:** it can be concluded that the salivary cortisol test tool can be used as an additional objective examination in order to check stress conditions in workers, in addition to a subjective examination like a questionnaire or anamnesis on workers. It is used for a biomonitoring effect and susceptibility biomonitoring. This salivary cortisol test can also be used to help determine stress levels in workers in order to detect early occupational diseases associated with psychosocial hazards.

**Keywords:** biomonitoring, salivary cortisol, work-related stress

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## INTRODUCTION

Stress is a condition that must be paid attention to by workers and employers, and therefore this condition if not treated can harm workers and reduce performance, which will eventually hamper the productivity services. 87% of the workers from Europe claimed that they suffered from stress in the workplace and 10% claimed they always had stress during their job. In 2015 around 28% of the workers reported suffering from work-related stress, with 33% clinical manifestations of fatigue, 19% sleep disturbances and 18% anxiety (Russell *et al*., 2018).

In Indonesia based on research in Sulawesi,19% of nurses in hospital suffered from heavy stress (Budiyanto, Rattu and Umboh, 2019) and based on another research in a Healthcare and Social Security Agency (BPJS kesehatan) in Semarang there were 46% of workers who experienced work stress (Mayang, Lestantyo and Kurniawan, 2018).

Stress will have a negative impact on general workers as well as employers. Impacts that can affect workers can be absenteeism (Holmgren *et al*., 2016) and presenteeism (Kim *et al*., 2019). Diagnosing work related stress is not easy because many factors will affect this condition, In terms of high job stressors, the possibility of stressors from outside the work must be minimized, and there should be assessment on how each worker accepts these stressors. This is also influenced by the ability of workers in coping mechanisms against the stressor itself. Following this, an objective measurement to workers as a supporting test can be made.

There are quite a lot of examinations that can be done to determine the level of stress in workers, but the majority of examinations are carried out using stressor questionnaires such as Survey diagnostic Stress (Widianti and Mardhiyah, 2017) and perceived stress questionnaires like perceived stress scale or PSS (Liu *et al*., 2020). On the other hand, objective tests like Heart Rate Variability test and Cortisol test for stress are still limited. Based on this background, in this research the researchers made an evidence-based case report to further examine one of the newest objective tests for stress, namely salivary cortisol to examine work-related stress.

***Cite this as:*** Aditya, M. R and Ilyas, M. (2022) 'Examination of Salivary Cortisol as a Biomonitoring of Work-Related Stress', *The Indonesian Journal of Occupational Safety and Health*, 11(1), pp. 152-160.

 doi:10.20473/ijosh.v11i1.2022.152-160
Received February 10, 2021, received in revised form May 26, 2021, Accepted December 08, 2021, Published: April 2022

## METHODS

A literature review was conducted on November 23, 2020 through searches on PubMed, Cochrane, and Google Scholar databases to find all published observational studies evaluating the relationship between salivary cortisol and work-related stress. Furthermore, the researchers conducted searches using the keywords listed in Table 1, with the inclusion criteria including the use of English language, free full texts, worker subjects, diagnostic studies, and comparisons with other test tools. The process of article selection is presented in Figure 1. The selected journals would have a diagnostic study critical appraisal using the worksheet from the Centre for Evidence-Based Medicine (CEBM), University of Oxford .

**Table 1.** Search Strategy Using Keywords

| Database | Keyword | Hints | Filter |
|---|---|---|---|
| Pubmed | ("specificity and sensitivity"[Title/Abstract] OR "sensitivity and specificity"[MeSH Terms]) AND ("cortisol"[Title/Abstract] OR cortisol[MeSH Terms]) AND ("workers"[Title/Abstract] OR "occupational groups"[MeSH Terms]) AND ("stress"[Title/Abstract] OR "burnout"[Title/Abstract] OR "burnout, professional"[MeSH Terms]) | 11 | Title/ abstract and Mesh term |
| Pubmed | ((("work related stress"[Title/Abstract]) OR (work related stress [MeSH Terms]))) AND (((((("workers"[Title/Abstract])) OR ("employee"[Title/Abstract])) OR (workers[MeSH Terms])) OR (employee[MeSH Terms]))) AND (("salivary cortisol"[Title/Abstract]) OR (salivary cortisol[MeSH Terms])) | 33 | Title/ abstract and Mesh term |
| Cochrane | "#1 - (workers):ti,ab,kw AND (salivary cortisol):ti,ab,kw AND ("Occupational Stress Indicator"):ti,ab,kw" | 0 | Title/ abstract |
| Google scholar | Work related stress and salivary cortisol | 10 | Title |

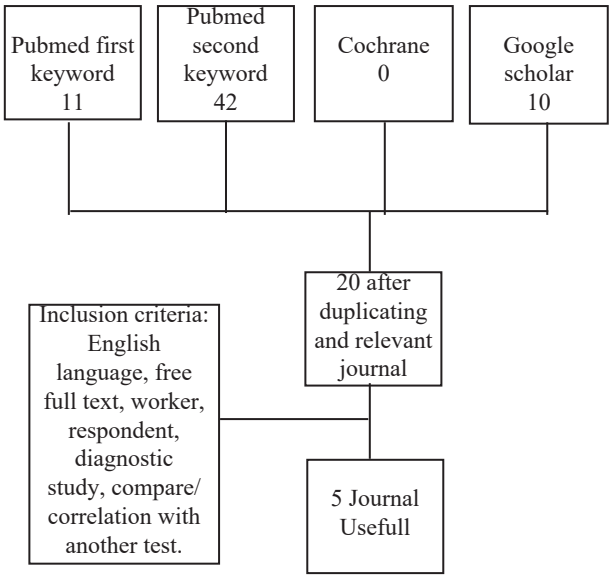


**Figure 1.** Article Selection Strategy

## RESULTS

After screening using inclusion criteria and reducing the duplication of articles, 5 articles were obtained. The first article in 2017 described the relationship between cortisol levels in saliva and the work location in the emergency dispatcher teams (Bedini *et al*., 2017). The second research article overall assessed the relationship between cortisol in saliva, cytokines, and job stress in oil and gas workers in 2020 (Reale *et al*., 2020). The third article investigated medical workers as one of the many workers who had high occupational stress. This article explained about the correlation between subjective psychological assessment and salivary cortisol as one of the biomarkers of stress in humans (Deneva, Ianakiev and Keskinova, 2019). The fourth article in general aimed to look at the validity and reliability of the Imperial Stress Assessment Tool (ISAT) in assessing the stress level of the surgical doctors, including the accuracy rate of salivary cortisol compared to the ISAT (Arora *et al*., 2010). The last article aimed at comparing the results of salivary cortisol with work stress conditions in patients who had been assessed in advance by a psychiatric specialist using the DSM IV criteria (Pilger *et al*., 2018).

Of the 5 selected journals, a critical appraisal was performed using the diagnostic study appraisal worksheet which can be seen in Table 2 with four levels of evidence, consisting of:

Level 1: Systemic review of cross sectional studies with consistently applied reference standard and blinding. Level 2: Individual cross sectional

studies with consistently applied reference standard and blinding. Level 3: Non-consecutive studies, or studies without consistently applied reference standards. Level 4: Case control studies or "poor or non independent reference standard"

The first journal aimed to objectively assessed stress levels by examining cortisol in saliva in workers as medical operators in emergencies, and investigating its relationship with stress perception and several other variables including type of workshift in 22 respondents with randomized shift control trial. Researchers used a visual analogue scale (VAS). Perceived stress was measured at the same time as the first saliva sampling during the three types of shifts, and the results showed that cortisol levels at the endpoint had a higher inclination for incoming emergency call shift than re-assessment and dispatch shifts. The mechanism of cortisol degrees elevated with bigger perceived stress either in both overall and each shift (Bedini *et al*., 2017).

The second journal written by Reale *et al*. (2020) aimed to assess correlation between work-related stress and salivary cortisol in 80 oil and gas company workers using a cross sectional design. Work-related stress was assessed by the state-trait-anxiety inventory (STAI) and job stress questionnaires. The results showed that the decision latitude ($P<0.001$), Job Demand ($p<0.05$) and Job strain ($p<0.001$) showed a statistically significant difference between the group with salivary cortisol and without salivary cortisol (Reale *et al*., 2020).

A journal with a total of 303 respondents working as physicians at the University Hospital St. George aimed at analyzing the relationship between blood serum levels of cortisol, salivary cortisol and another biomarker with burnout syndrome in physicians with different medical specialties. using the cross-sectional design study. The author has found that Saliva cortisol in the burnout cluster was significantly higher than that in the control cluster and no burnout group ($P<0.05$) (Arora *et al*., 2010).

The fourth journal which involved 54 observations on 11 surgeons aimed at presenting the sensitivity and specificity of salivary cortisol compared to STAI as a baseline/ reference test. Based on this journal STAI had reliability for use in these respondents (Alpha Cronbach>0.6). The result showed that salivary cortisol had sensitivity 70%, specificity 90%, PPV 88%, NPV 75% and LR(+) 7.78. Based on the value of LR(+), the salivary

**Table 2.** Critical Appraisal

| **Journal 1** | |
|---|---|
| **Level of evidence** | **Level 3** |
| "Was the diagnostic test evaluated in a representative spectrum of, patients? | Yes, the researchers recruited 22 phone operators and an RCT for each phone operator. All outcome information remained blinded until the termination of the study. |
| Was the reference standard applied regardless of,the index test result? " | Yes, the researchers used VAS (visual analogue scale). Perceived stress was measured simultaneously as the first saliva sampling |
| Was there an independent, blind comparison between the index test,and an appropriate reference ('gold') standard of diagnosis? " | Yes, cortisol was measured using an enzyme-linked-immunosorbent serologic assay kit, and the respondents had to fill out the questionnaires without knowing the results of the salivary cortisol test. |
| Are test characteristics,presented?" | Unclear. In the results section, the researchers only presented the results in the form of numerical data, so based on these data only the correlation between 2 tests above could be concluded.<br>Baseline:<br>The level of cortisol at the endpoint had an inclination to be higher for incoming emergency call shift than re-assessment and dispatch shifts.<br>Longitudinal:<br>The mechanism of cortisol degrees elevated with bigger perceived stress in both overall and each shift. |
| "Were the methods for performing the test described in sufficient detail to permit, replication? | Yes, in the section of Main outcome: Saliva cortisol |
| **Journal 2** | |
| **Level of evidence** | **level 2** |
| Was the diagnostic test evaluated in a Representative spectrum of, patients? | Yes,<br>an overall of 80 healthy employees had been recruited among a population of operators of gas and oil extraction. |
| Was the reference standard applied regardless of,the index test result? " | Yes, the researchers used state-trait-anxiety inventory (STAI) and job stress questionnaires considering job demand (JD), decision latitude (DL), social support (SS), job insecurity (JI), and job strain. |

**Continued Table 2.** Critical Appraisal

| Journal 2 | |
|---|---|
| **Level of evidence** | **Level 2** |
| "Was there an independent, blind comparison between the index test,and an appropriate reference ('gold') standard of diagnosis? " | Yes, cortisol was measured using a commercial (solid phase) ELISA Kit and the respondents had to fill out the questionnaires without knowing the results of the salivary cortisol test. |
| "Were test characteristics,presented?" | Unclear. In the results section, the researchers presented the results of cortisol in categorical data but for the index test in numerical form, so based on these data only the correlation between 2 tests above could be concluded. Baseline: Decision latitude (DL), Job Demand (JD) and Job strain were shown. |
| Were the methods for performing the test described in sufficient detail to permit, replication? | Yes, in the Saliva Sampling and Cortisol Analysis section. All saliva samples of all registered staff were collected at 8:00 am / between one hour of awakening |
| **Journal 3** | |
| **Level of evidence** | **level 2** |
| Was the diagnostic test evaluated in a Representative spectrum of, patients? | Yes, 303 physicians employed in hospital were used as a comparison group of 111 people working outside. The medicine was used as iControl to verify the results. |
| Was the reference standard applied regardless of,the index test result? " | Yes, the researchers used the Maslach Burnout Inventory (MBI) to identify burnout symptoms. This instrument is at present the most frequently used instrument for evaluating burnout in health care professionals. |
| "Was there an independent, blind comparison between the index test,and an appropriate reference ('gold') standard of diagnosis? " | Yes, every subject had to fill out the MBI first, and after that the subjects had to undergo a salivary cortisol test |

**Continued Table 2.** Critical Appraisal

| Journal 3 | |
|---|---|
| **Level of evidence** | **Level 2** |
| "Are test characteristics,presented?" | Unclear. In the results section, the researchers presented the results in categorical data but for the index test in numerical form, so based on these dataonly the correlation between 2 tests above could be concluded. Saliva cortisol in the burnout group was significantly higher than that in the control group and no burnout group (P<0.05). |
| Were the methods for performing the test described in sufficient detail to permit, replication? | Yes, in the salivary cortisol collection section. |
| **Journal 4** | |
| **Level of evidence** | **level 2** |
| Was the diagnostic test evaluated in a Representative spectrum of, patients? | Yes, in the sections of participants and procedures observed. The researchers assessed 54 perceptions in 11 registered specialists from the general, cardiothoracic, and injury and orthopedic surgery divisions. |
| Was the reference standard applied regardless of,the index test result? | Yes, STAI (subjective perception) was used as the baseline or gold standard. |
| Was there an independent, blind comparison between the index test,and an appropriate reference ('gold') standard of diagnosis? | Yes, every subject had to fill out questionnaires first, and after that the subjects had to undergo a salivary cortisol test |
| Are test characteristics,presented?" | Yes, Sensitivity = 70% Specificity = 91% Positive predictive value(PPV)= 88% Negative predictive Value(NPV)= 75% Likelihood ratio(+) / LR(+) =7.78 |
| Were the methods for performing the test described in sufficient detail to permit, replication? " | Yes, in the salivary cortisol section: Collection and measurement before and after the procedure |

**Continued Table 2.** Critical Appraisal

| Journal 4 | |
|---|---|
| **Level of evidence** | **Level 2** |
| Were the methods for performing the test described in sufficient detail to permit, replication? | Yes, in the salivary cortisol section: Collection and measurement before and after the procedure |
| **Journal 5** | |
| **Level of evidence** | **level 2** |
| Was the diagnostic test evaluated in a Representative spectrum of, patients? | Yes, in the patient recruitment section, and the study design involved 66 respondents divided into 2 groups, namely the burnout/stress group and control group. |
| Was the reference standard applied regardless of,the index test result? | Yes, in the clinical axis I, the main diagnoses were assessed in line with DSM-IV |
| Was there an independent, blind comparison between the index test,and an appropriate reference ('gold') standard of diagnosis? | Yes |
| Are test characteristics,presented? | Unclear. In the results section, the researchers presented the results of the reference test in the form of categorical data but for the index test in numerical form, so based on these data only the correlation between 2 tests above could be concluded.<br>Baseline:<br>Efficient cortisol levels as total salivary cortisol after awakening (P adjusted <0.05)<br>Longitudinal study:<br>After the psychosocial treatment,,the temporal developments of midday cortisol and saliva cortisol nadir, showed a significant statistical interaction with the group variables. |
| Were the methods for performing the test described in sufficient detail to permit, replication? | Yes, in the section of Salivary Cortisol: Collection and Measurement |

of cortisol in saliva and assessing its correlation with burnout in hospital workers. The burnout was diagnosed by a mental health specialist based on the DSM IV diagnostic criteria. The results showed that there was a correlation between the increased cortisol in saliva, especially the increase that occurred upon awakening (Pilger *et al*., 2018).

## DISCUSSION

Cortisol is one of the most important glucocorticoids produced in the zona fasciculata of the adrenal cortex. The hypothalamic hormone CRH and the pituitary hormone ACTH control cortisol secretion in the hypothalamus-pituitary-adrenal axis.

Cortisol is a stress hormone that plays a role in the body's response to physical and/or mental stress. Cortisol also helps to maintain homeostasis by regulating blood pressure, the immune system, protein, carbohydrate, fat metabolism, and anti-inflammatory activity. Cortisol deficiency causes Addison's disease, whereas cortisol overproduction causes Cushing's syndrome (Katsu and Iguchi, 2016).

When a person is faced with a stressor, the body automatically activates the HPA-axis system with the initial goal of stimulating the body to respond to that stressor, which is basically a good response. The HPA axis is activated through the association cortex, amygdala, and hippocampus, causing an increase in production. CRH thus stimulates the pituitary gland to produce ACTH.

The ACTH will go to the adrenal glands to produce the hormone cortisol, resulting in an increase in cortisol in the blood. As previously stated, the hormone cortisol is basically good for stimulating "awake" in the human body, but if the stressor is given in excess there will be excessive cortisol levels in the body. This causes adverse effects in the body both physically and physically. Psychological effects include stress(Cay *et al*., 2018).

Sleep has an effect on cortisol's circadian cycle. Cortisol levels in either serum, urine or saliva physiologically are lower at the start of sleep, but

the levels rise towards the end, hitting the peak only minutes before the person wakes up, according to normal physiology. The sleep–wakefulness cycle helps to create this rhythm (Mohd Azmi *et al*., 2021).

There are several terms and conditions in carrying out the cortisol test in saliva, especially things that the patients must do. Before taking the sample, the patients should refrain from using any steroid inhalers for at least 24 hours, and from using steroid creams or lotions, such as hydrocortisone. Moreover, if the gums or the inside of the mouth is bleeding, sampling should not be carried out.

Children under the age of three should not use a saliva collection device, and an adult should assist children under the age of ten. Prior to obtaining the sample, teeth also should not be cleaned or flossed. Moreover, 30 minutes before taking the sample, patients are not allowed to eat or drink anything and to use their fingers to contact the swab. If the patients have one or both of these issues frequently, they should speak with a doctor (Allina Health, 2019).

Stress is the body's reaction to a cause of stress, also known as a stressor, and it can have a psychological and physiological impact on the body (Gaol, 2016). The stress response model is a hypothesis regarding stress that was initially proposed by Hans Sely (Tan and Yip, 2018) based on his findings. The stress response model is a hypothesis that states that stress is an individual's response to a stimulus, and this is a specific response to a stimulus that can have an impact on life.

According to the World Health Organization, work-related stress is a reaction that a person has in response to expectations and pressures at work that are greater than the worker's capacity to handle (World Health Organization, 2020). Based on the review of the 5 journals above, there are good results showing that the salivary cortisol examination is significantly associated with several subjective examinations, both in the form of questionnaires like VAS, Maslach Burnout Inventory, Job Stress Questionnaire and a direct assessment of axis 1 psychiatric diagnosis conducted by a psychiatric specialist.

There is 1 study that presented the results of the accuracy of the salivary cortisol test after being compared with STAI, which had a fairly good reliability value. The results presented show that sensitivity 70% means that 70% of subjects who had stress were detected in this test, and specificity 91% means that 91% of subjcts without stress would have a negative test.

A positive predictive value of 88% means that 88% of the population had a positive test result, and they truly had stress. NPV 75% means 75% of population had a negative test result, and they truly had no stress. Moreover, likelihood ratio (+) 7.78 means this test was moderately good enough for assessing stress in workers (Arora *et al*., 2010).

Based on a study from China, cortisol concentration in saliva was correlated with occupational stress and gradually increased with the increasing degree of stress (Tian *et al*., 2016). Other studies have shown that salivary cortisol levels could be used as a predictor of stress in workers (Susoliakova *et al*., 2018).

It should be noted that the 2 previously mentioned studies used subjective stress questionnaires, with the aim to confirm that this salivary cortisol test could be used with other subjective tests such as questionnaires to detect job stress in workers.

A study in the UAE concluded that the evaluation of cortisol ranges and subjective pressure could assist to discover groups with impaired reaction to stress and increase cortisol stages (Bani-Issa *et al*., 2020). In Giza, the researchers showed that workers that did not have stress had a significantly lower cortisol level than employees group that might suffer from acute state of stress (Amer and Monir, 2018). Another study said that salivary cortisol was shown to significantly decrease in stressed patients with interventions provided by health workers(Ornek and Esin, 2020).

The availability of cortisol salivary test in Indonesia has been recorded in several laboratories, and the facilities can be used by both workers and non-workers to detect stress conditions. The fact that salivary cortisol examination can be done in Indonesia is based on the information contained in research in Surabaya, East Java (Sulfiana, Tualeka and Widajati, 2018) and in other studies using salivary cortisol examination carried out in a laboratory in Malang, East Java (Nagara, Alamsyah and Triyuliarto, 2019). However, so far the salivary cortisol examination has only been used for research in several laboratories. It is expected that salivary cortisol can used for daily activity of occupational health practices in the near future.

The best time to assess work-related stress is an awakening cortisol because the cortisol sample in saliva in the morning has a low level of bias due to

the absence of any acute stressors upon awakening in the morning. If it turns out that high cortisol levels are found when someone wakes up in the morning with a note regarding the criteria for adequate sleep, it can be said that humans experience anticipatory stress which is quite often experienced by workers, especially on weekdays (MacDonald and Wetherell, 2019).

CAR values are also proven in other studies showing a decrease in workers who had been given interventions at work regarding work stress (Almeida *et al*., 2018). The reference results were based on the kit product, which was an ELISA kit. The reference result of adults was 0.12–1.47 µg/dL (DRG Instruments GmbH, 2016).

The cortisol awakening response (CAR) is a unique aspect of the circadian cortisol rhythm, characterized by a rise in cortisol within the first hour after awakening, which is different from the cortisol increase at night (Elder *et al*., 2016). Because it is controlled differently from cortisol output during the remainder of the diurnal cycle, the CAR has emerged as a crucial component of hypothalamic-pituitary-adrenocortical axis function. Stress, emotional problems, and physical health risks have also been linked to it (Steptoe and Serwinski, 2016).

A greater cortisol awakening response (CAR) substantially predicted enhanced initial onset of anxiety disorder, and a higher CAR was also a strong and significant predictor of the subgroup of social anxiety disorder onset (Adam *et al*., 2014).

A CAR might be a good way to prepare for a stressful situation. When coping with hazardous events, emotional memory circuits may change the CAR and contribute to resilient or susceptible behaviors (Contreras and Gutierrez-Garcia, 2018).

Stress at work which a patient experiences continuously or chronically every day and the level of cortisol will increase more than normal in the morning when the patient begins to do his work activities. This statement is in accordance with the stress anticipation hypothesis.

Cortisol salivary test is one of the objective tests to assess stress condition in every situation. CAR or cortisol awakening response in research that was conducted by Boggero (Boggero *et al*., 2017) was shown to be sensitive index to assess the psychological response to psychological stresor. Thus, if the assessment of work-related stress to workers is needed, screening for the stressor in the workers should be carried out first to make sure that the stressor comes from the workplace. After that, to make sure the worker condition, a biological test like salivary cortisol test can be carried out. In line with Giovanni's research, in interpreting the results of salivary cortisol, it is necessary to assess the type of stressor experienced by workers to produce an appropriate interpretation (Bani-Issa *et al*., 2020).

Based on research that was conducted in Czech, salivary cortisol levels are an excellent objective measure of stress which can be utilized by public health agencies as a good predictor of occupational stress for primary prevention (Susoliakova *et al*., 2018). However, this is not in line with research conducted on Canadian employees, which stated that there was no link between salivary cortisol levels and chronic stress experienced by workers. The absence of relationship in this study might be caused by the method and the small number of samples taken (Assis, Resende and Marziale, 2018).

The positive feature of the five journals that have been selected is that all of the journals assessed used worker respondents, and all also showed that the salivary cortisol test had the ability to objectively assess the stress level of workers. In addition, the journals used are still in the last 10 years, and only 1 journal is more than 5 years old. The weakness of the 5 journals selected in this study is that there is only 1 journal that presented data on the accuracy of the salivary cortisol test kit, so that in determining the specificity and sensitivity of the tool it is only based on 1 journal. Meanwhile, the rest only presented the level of correlation with subjective examinations that have been commonly used so far for assessing work-related stress.

## CONCLUSION

Work-related stress is a condition that is very detrimental to both workers and employers. Detecting work-related stress conditions is a fairly complicated examination. The salivary cortisol test can be used as an additional examination in order to objectively check stress conditions in workers in addition to a subjective examination like a questionnaire or anamnesis on workers. The use of salivary cortisol test can be used as a biomonitoring on workers, both as a biomonitoring effect and a susceptibility biomonitoring. This salivary cortisol test can also be used to help determine stress levels in workers in order to detect early occupational diseases associated with psychosocial hazards.

## ACKNOWLEDGEMENTS

The authors would like to send the greatest gratitude to Allah SWT. We also would like to thank the supervisors and family for their support for the publication of this article.

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