Occupational Risk Factors for Musculoskeletal Disorders among Operation Room Nurses at Cairo University Hospitals

Gehad Abo El Ata¹, Eman Khalifa¹, Soha El Desouky², Dina Sabry³ and Marie Manawil¹*

¹Department of Occupational and Environmental Medicine, Cairo University, Egypt.
²Department of Rheumatology and Rehabilitation, Cairo University, Egypt.
³Department of Biochemistry and Molecular Biology, Cairo University, Egypt.

Authors' contributions

This work was carried out in collaboration between all authors. Author GAEA designed the study and revised every step during work. Author EK wrote the protocol, managed the field study and analyzed the results. Author SED managed the clinical part in the study. Author DS performed the chemical analysis of the biomarker CTX-II and author MM wrote the first draft of the manuscript and managed the literature researches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/24634

ABSTRACT

Aims: To assess the occupational risk factors that contribute to the occurrence of work-related musculoskeletal disorders among Operation Room (OR) nurses and MSDs relation to biomarker c-telopeptide of type II collagen (CTX-II).

Study Design: A cross sectional study.

Place and Duration of Study: Cairo University hospitals from January to April 2014.

Methodology: The study was conducted upon 184 OR nurses from different specialties. They include 155 females and 29 males with age ranged 20-50 years and work duration ranged 2-35 years. They represent 52.6% of the OR nurses work power all over Cairo University hospitals. The
individuals were subjected to questionnaires including Standardized Nordic Questionnaire (SNQ), Job Content Questionnaire (JCQ) and Quick Exposure Check (QEC) for ergonomic risk assessment. Urinary CTX-II was measured.

Results: Out of 184 OR nurses, 180 have musculoskeletal symptoms with a prevalence of 97.8%. CTX-II in females was non-statistically significant higher than in males. Higher non-statistically significant levels of CTX-II were found in those aged ≥ 40 years than in those < 40. Non-statistically significant differences were in correlation between CTX-II and various occupational risk factors as BMI, age, duration of employment, physical risk factors except for outreached arm ($r=0.16$, $p=0.03$) and psychosocial factors except for deficient rest break ($r=-0.15$, $p=0.038$) which showed statistically significant differences. No statistically significant correlation was found between CTX-II and any of musculoskeletal symptoms during the past twelve months by applying SNQ. A statistically significant difference ($Z=2.26$, $p=0.02$) was found in OR nurses group with knee crepitus in comparison with nurses group without knee crepitus among those with high level of urinary CTX-II. Other MSDs showed no statistically significant differences between symptomatizing and non-symptomatizing groups.

Conclusion: Operating room nurses are exposed to multiple occupational risk factors leading to MSDs. CTX-II may be a valuable biomarker in early osteoarthritis.

Keywords: MSDs; operation room nurses; occupational risk factors; CTX-II.

1. INTRODUCTION

Musculoskeletal disorders are reported to significantly impact the quality of life, cause lost work time or absenteeism, increase work restriction, transfer to another job, or disability than any other group of diseases [1].

Musculoskeletal disorders are considered as multifactorial disorders, there are multiple work related risk factors implicated in their development, or exacerbation [2]. Therefore, effective application of ergonomics in work system design can achieve a balance between worker characteristics and task demands [3].

Among hospital nurses, operating room nurses are considered a high risky group. Operating room nurses are exposed to a variety of risk factors that are responsible for disorders of musculoskeletal system. The factors include static posture (e.g. prolonged standing and trunk and neck flexion), awkward posture of the trunk and manual handling (e.g. lifting instruments and heavy objects, pulling/pushing heavy equipment and patients’ trolleys) [4].

Recently efforts have focused on the use of sensitive biochemical markers of cartilage degradation for early diagnosis of joint affection and osteoarthritis [5].

Measurement of carboxyl-terminal cross-linked telopeptide of type II collagen (CTX-II), as a biomarker has been associated with cartilage turnover and its urinary excretion has been shown to increase in case of osteoarthritis [6].

This work aims at assessing the psychosocial, organizational and physical ergonomic occupational risk factors that contribute to the occurrence of MSDs among operating room nurses. The current study aims also to search for a relation between a biomarker CTX-II and MSDs risk factors as a biomarker of early cartilage degradation.

2. METHODOLOGY

2.1 Subjects

This study is cross sectional. The study took place at big Egyptian teaching hospitals (Cairo University hospitals) over the first 4 months in 2014. It was conducted upon 184 Operating Room (OR) nurses from different specialties representing 52.6% of the OR nurses work power all over the hospital. The participant nurses met the inclusion criteria with age ≤ 50 years and body mass index (BMI) ≤ 30 kg/m².

Exclusion criteria were: diabetes mellitus, obesity with BMI > 30 kg/m², rheumatoid arthritis, varicose veins as well as history of recent trauma or fracture within the last year.

2.2 Methods

The included group was subjected to a full personal, occupational and medical history
Clinical examination was performed to the subjects with special emphasis on musculoskeletal system examination.

An Arabic version of the Standardized Nordic Questionnaire (SNQ) of musculoskeletal disorders was used to report cases presenting with MSDs among the study population. It shows a body map diagram of nine anatomic regions which are neck, shoulders/arms, elbows, wrists/hands, upper back, lower back, hips/thighs, knees and ankles/feet and ask about presence of any troubles (pain, ache and discomfort) during the last twelve months and past seven days, prior to the interview, in each of the body areas. It also assesses the severity of symptoms by asking about presence of any musculoskeletal troubles during the last twelve months, prior to the interview, that preventing normal work at home or away from home [7].

To help the detection of risk factors of WMSDs development, the study used two questionnaires: Job Content Questionnaire (JCQ) and Quick Exposure Check (QEC).

The minimum core Job Content Questionnaire (JCQ) is the used tool to measure social and psychological characteristics of job and to find if there is work related psychosocial risk factors. This questionnaire consists of twenty seven questions about job decision latitude scale which are the sum of two subscales: Job skill discretion and decision authority; job demands; social support; and job insecurity. Each item was scored based on a four-point scale (i.e., strongly agree to strongly disagree or often to never) [8].

The following are Job Content Questionnaire scales scoring and average

| Scoring            | Average |
|--------------------|---------|
| Job skill discretion | 33.3    |
| Job decision-making authority | 36.8    |
| Job demands        | 30.9    |
| Decision latitude  | 70.3    |
| A job strain ratio | ≤ 1     |
| Co-worker support  | 12.73   |
| Supervisor support | 11.94   |
| Total social support | 24.6   |
| Job insecurity     | 4.91    |

Quick Exposure Check (QEC) is used for ergonomic risk exposure assessment and to provide a basis for ergonomic interventions. It is a one-page assessment sheet which includes questions for both the practitioner (observer) and the worker. The observational part was used to assess of posture and movement of the back, shoulder/arm, wrist/hand and neck. The part of workers questions, the worker has to answer several questions about work related physical risk factors as maximum weight handled, maximum force level, time spent on task, visual demands, presence of vibration, work pace and stress. For each question shading was placed in the most appropriate box. The graduation in shading for each question indicates an increase of exposure to risk [9].

### Ergonomic risk assessment scores of QEC

| Risk Rating (RR) | Low | Moderate | High | Very high |
|------------------|-----|----------|------|-----------|
|                  |     | Assessment scores |
| Back             | 10-20| 21-30 | 31-40 | 41-56     |
| Shoulder/Arm     | 10-20| 21-30 | 31-40 | 41-56     |
| Wrist/Hand       | 10-20| 21-30 | 31-40 | 41-56     |
| Neck             | 2-6  | 7-10   | 11-14 | 15-18     |
| Vibration        | 1    | 4      | 9     | -         |
| Work Pace        | 1    | 4      | 9     | -         |
| Stress           | 1    | 4      | 9     | -         |
|                  | 1    | 4      | 9     | 16        |

### 2.3 Laboratory Investigation

#### 2.3.1 Urine sample collection and preparation

From each subject 10 cc of urine was collected into clean dry containers under complete aseptic conditions for determination of urinary CTX-II. Each sample collected was transported to the laboratory on the same day within two hours and kept frozen at -20°C until assayed.
2.3.2 Urinary c-telopeptide collagen type II

Type II collagen degradation which reflect cartilage turnover was assessed by measuring CTX-II using an enzyme linked immunosorbant assay (ELISA). Human galactomannan (GM) ELISA kit (Glory Science Co.) was used.

2.3.3 Principle of test

The kit is for quantitative level of GM to wells, combine GM antibody with labeled HRP to form antibody – antigen – enzyme – antibody complex, after washing completely, add TMB substrate solution, TMB substrate become blue color at HRP enzyme catalyzed, reaction is terminated by the addition of a stop solution and the color change is measured at a wavelength of 450 nm. The concentration of GM in the samples is then determined by comparing the O.D. of the samples to the standard curve.

2.4 Statistical Analysis

Data were statistically described in terms of mean ± standard deviation (±SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann Whitney U test for independent samples when comparing 2 groups. For comparing categorical data, Chi square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using Spearman rank correlation equation. $p$ values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

3. RESULTS AND DISCUSSION

3.1 Results

The sociodemographic and occupational characteristics of the studied population are shown in Table 1. The study was conducted upon 184 OR nurses from different specialties. They include 155 females and 29 males. The majority of them are females (84.2%). The ages of the study group ranged from 20-50 years with mean age is 36.12±8.15 years. The majority of them (60.9%) are below the age of 40 years. Most of the study group (78.3%) are overweight which means that their BMI ranged from 25 - 29.9 kg/m². Their duration of work ranged from 2 to 35 years with mean 17.32±8.080 years. The working hours/ week ranged from 36-60 hours with mean 38.28±4.764. They are overloaded at work with the overall patient-to-nurse ratio per shift is considered high ranged 2 - 25 with mean value of 8.84±4.71 patient/shift.

On assessment of ergonomic risk among the study population, Quick Exposure Check (QEC) is used to show percentage of ergonomic risk rating exposure as plotted in Fig. 1.

Most of the study group shows that back risk is very high (44.6%), shoulder/arm risk is either high or very high with equal percentage (34.8%), wrist/hand is moderate (43.5%). Neck risk is very high representing 51.6%, job stress risk is also very high (54.3%), work pace risk is moderate (66.8%), while vibration risk is low among 65.8% of the studied group.

On applying the Job Content Questionnaire (JCQ) on OR nurses participated in the study, the majority shows normal job skill discretion (52.7%), low decision authority (83.7%), low decision latitude (73.4%) with high job demand (82.6%) and job strain was found in (62%) of the group. Also, there is low social support representing (79.9%) and the job insecurity is low (51.6%). The Percentages of normal and abnormal scores of scales of JCQ among OR nurses are shown in Fig. 2.

Biomarker CTX-II levels are compared in females with males operating room nurses in Table 2. This comparison shows that the levels in females are higher than in males but not to a statistically significant level. When comparing the biomarker levels according to age, higher levels are found in those aged 40 years or more than in those below 40 years but also not to a statistically significant level. These comparisons are according to Mann-Whitney test ($p > 0.05$). Correlations between CTX-II and various occupational risk factors are shown in Table 3. Non statistically significant differences are found as regards BMI, age, duration of employment, physical risk factors except for outreached arm and psychosocial risk factors except for deficient rest break which show a statistically significant difference.
Table 1. Sociodemographic and occupational characteristics in the studied population (n= 184)

| The studied population parameters | Range  | Mean ± SD  |
|----------------------------------|--------|------------|
| Age (years)                      | 20-50  | 36.12±8.145 |
| Weight (Kg)                      | 50-100 | 73.57±9.969 |
| Height (Cm)                      | 150-190| 165.17±7.798 |
| Body Mass Index (BMI)            | 19.5-29.8| 26.934±2.5694 |
| Duration of employment (years)   | 2-35   | 17.32±8.080 |
| Daily working hours/ week        | 36-60  | 38.28±4.764 |
| Standing hours/ shift            | 1-10   | 5.14±1.950 |
| Patient nurse ratio              | 2-25   | 8.84±4.715  |

Fig. 1. Percentage of ergonomic risk rating exposure among OR nurses using Quick Exposure Check (QEC) for ergonomic risk assessment

Table 2. Mean values (±SD) of urinary CTX-II level among the studied group according to age and gender using Mann-Whitney test

| CTX-II * (Mean ± SD) | Z score | P value § |
|----------------------|---------|-----------|
| Male (n=29)           | 594.90±450.639 | -0.171 | 0.864 |
| Female (n=155)        | 602.97±438.386  | -0.304 | 0.76 |
| Age < 40 y.           | 601.14 ± 424.3 | -0.022 | 0.987 |
| Age ≥ 40 y.           | 602.57 ± 464.22 | -0.019 | 0.990 |
| Total                | 601.70 ± 439.099 | -0.022 | 0.987 |

* urinary CTX-II is measured in µg/L; § significance p<0.05

Correlations between musculoskeletal symptoms at the last 12 months using SNQ among the studied operation room nurses and the levels of urinary CTX-II are shown in Fig. 3. It shows that there is no statistically significant correlation between urinary CTX-II level and any of musculoskeletal symptoms during the last 12 months (p> 0.05). Results show correlations between CTX-II and symptoms at each of different body regions are as follows: at neck (r=0.043, p=0.560), at shoulders and arms (r=0.034, p=0.646), at elbows (r= -0.022, p=0.770), at wrists and hands (r= -0.019, p=0.797), at upper back (r=0.137, p=0.064), at lower back (r=0.043, p=0.559), at hips (r=0.112, p=0.128), at knees (r=0.045, p=0.540) and at ankles and feet (r=0.086, p=0.246).
Fig. 2. Percentage of normal and abnormal scores of scales of job content questionnaire among OR nurses participated in the study.

Fig. 3. Correlation of symptoms at different body regions with biomarker CTX-II.

Comparing the OR nurses group with MSDs symptoms and signs with the OR nurses group without MSDs among those with high level of urinary CTX-II using Mann-Whitney test is shown in Table 4. A statistically significant difference was found in OR nurses group with knee crepitus in comparison with the group without knee crepitus (p<0.05). While the other musculoskeletal symptoms and signs show no statistically significant differences between symptomatizing and non-symptomatizing groups among those with high level of CTX-II (p>0.05).
Table 3. Spearman correlation between personal, physical and psychological risk factors and urinary CTX-II level among the studied operation room nurses

| Risk factors                        | Urinary CTX-II |
|------------------------------------|----------------|
|                                    | r   | p        |
| Age                                | 0.030 | 0.684   |
| Body mass index (BMI)              | 0.058 | 0.433   |
| Duration of employment             | 0.026 | 0.730   |
| Standing hours                      | 0.071 | 0.335   |
| Awkward posture                    | 0.035 | 0.637   |
| Moving/lifting heavy objects       | 0.076 | 0.304   |
| Pushing/ pulling heavy objects     | -0.004 | 0.960   |
| Repetitive shoulder movement       | 0.081 | 0.276   |
| Repetitive wrist movement          | -0.054 | 0.467   |
| Outreached arm                     | 0.160 | 0.030*  |
| Neck bending                       | 0.050 | 0.499   |
| Deficient rest break               | -0.153 | 0.038*  |
| Inadequate number of workers       | -0.077 | 0.296   |

*significance p<0.05

Table 4. Comparison between the OR nurses group with MSDs and the OR nurses group without MSDs among those (75% of nurses. n=138) with high levels of urinary CTX-II using Mann-Whitney test

| The 2 groups of OR nurses with high levels of urinary CTX-II (>200µg/L) | Musculoskeletal symptoms and signs among nurses | Z score | P-value |
|-----------------------------------------------------------------------|------------------------------------------------|---------|---------|
| Knee crepitus                                                         | 2.264                                          | 0.024*  |
| Joint effusion                                                        | 7.17                                           | 0.473   |
| Joint tenderness                                                      | 1.369                                          | 0.171   |
| Tingling of back of thigh                                            | 1.659                                          | 0.097   |
| Tingling of hands and fingers                                         | 0.4                                            | 0.685   |

*significance p<0.05

3.2 Discussion

Considering the importance of MSDs as a public health problem, a study on this problem in OR nurses is a very important issue because musculoskeletal disorders is considered a significant occupational problem among healthcare providers [10,11].

Multiple occupational risk factors contribute in the development of MSDs among nurses in operating room. In the present study, the Quick Exposure Check (QEC) for ergonomic risk assessment is used for evaluation of work place situation, assessing, observing and measuring physical ergonomic stressors in the workplace. It is found that the level of exposure to ergonomic MSDs risk factors at majority is very high for back, shoulders, neck and stressful conditions, while it is moderate for wrists and work pace and low for vibration.

Operating room nurses are dealing with very exhausting, busy, and overloading work environment which requires more effort, so the organizational risk factors are very impressive. 162 nurses (representing 88.04% of the studied population) are overloaded due to inadequate number of workers. Lack of enough rest breaks due to time pressure and accelerated work rhythm in operation room environment has a bad impact on psychological condition and add more mental stress. Most of nurses showed abnormal scores in scales of Job Content Questionnaire (JCQ). A study used JCQ among patient care associates, nurses, and administrative personnel and found statistically significant associations between psychosocial demands and multi-site musculoskeletal pain [12].

Many studies depend on the level of CTX- II as a biochemical marker of cartilage tissue turnover and consider it an easy specific clinical tool for early diagnosis of OA [13-15]. Early osteoarthritis is often characterized by a molecular pre radiographic phase in which there is no structural joint changes [16], but only biochemical changes in joint tissues precede any clinical and radiographic finding of joint destruction [17,18].
The present study reveals that mean value of urinary level of CTX-II in the whole participants in the study is 601.70±439.099 µg/L. Urinary CTX-II level among the studied OR nurses ranged 66 – 1350 µg/L. High level of urinary CTX-II (> 200 µg/L) is present in 75% of the study group indicating presence of biological breakdown within articular cartilages, while the rest of participants (25%) show normal base line level of urinary CTX-II (≤ 200 µg/L) as compared with normal control during laboratory analysis to detect the cutoff level.

The presence of a positive correlation between age and urinary CTX-II level, even if not significant, reflects the presence of a well-known increase in prevalence of cartilage degradation with age. A study found that aging makes the joint more susceptible to the effects of OA risk factors that include abnormal biomechanics, joint injury and obesity [19]. Many studies found that CTX-II level does not increase significantly with age in OA patients [20,21].

The age of forty is the age at which clinical manifestations of osteoarthritis start to increase [22]. The majority of population in the present study (60.9%) are below the age of 40 years. In case of knee osteoarthritis which is the most common joint disease, it was found that it affects the middle aged and elderly. Osteoarthritic signs are uncommon in those aged ≤ 40 years [23,24]. The age of forty is a critical age for many health problems caused by shift work [25]. The present study reveals that CTX-II levels in females is higher than in males, however there is no statistically significant difference in the level of urinary CTX-II between males and females subjects. Another study showed similar results with no notable differences between men and women as regard CTX-II concentrations [26].

The present study finds that there is a positive but non-significant correlation between CTX-II levels and Body Mass Index (BMI) among the studied group. This finding is similar to a study conducted by Garnero and co-workers, in which they stated that body weight had no effect on the level of urinary CTX-II marker [27]. The results of the present study are in contrary to those reached by Mouritzen and co-workers, who found that subjects with a BMI >25 kg/m² have CTX-II concentrations significantly higher than in those with a BMI <25 kg/m² [25].

The correlations of CTX-II with occupational risk factors are positive, but non-significant except for two risk factors with significant correlation with CTX-II. These are outreached arm as a physical risk factor and inadequate rest break as a psychosocial risk factor.

A significant positive correlation is found between outreached arm and urinary CTX-II level, proving that this biomarker is helpful in diagnosis of upper extremity joint disorders and this result is supported by Saxton in a review of work-related upper extremity disorders, proposed a range of biomarkers, including those of collagen metabolism for early detection of such disorders [28].

Likewise, there is a statistically significant negative correlation between inadequate rest break and CTX-II level, meaning that lack of rest break during working day causes more exertion and effort and accordingly more stress and loading of joints and more articular destruction with release of CTX-II fragments into urine.

Out of 184 operation room nurses, 180 have musculoskeletal symptoms with a prevalence of 97.8%. The study group suffers from pain, tenderness over joints, swelling and joint effusion, limitation of movement and crepitus of knee joint which is a characteristic sign over knee joint only.

There is no statistically significant correlation between urinary levels CTX-II and any of musculoskeletal symptoms during the past twelve months by applying SNQ. Although it is non-significant, yet there is a positive correlation between CTX-II level and WMSD at neck, shoulders, upper back, lower back, hip, knees and ankles.

These results are concomitant with a study which was performed on patients fulfilling the American College for Rheumatology criteria for primary knee osteoarthritis. It was found that none of the associations between the Z scores of CTX-II and indices of pain, function or joint damage were significant [29].

The present study results reveal that there are no statistically significant differences in the level of urinary CTX-II between the group with symptoms and signs of OA like tenderness, joint effusion, limited joint mobility and tingling and numbness of thigh, when compared with the group without these manifestations among nurses with elevated CTX-II (>200 µg/L).
On the other hand, the present study results reveal that most nurses (75% of them) who had elevated CTX-II (>200 µg/L) show a statistically significant difference ($Z=2.26$, $p=0.02$) on comparing a group of nurses having knee crepitus with another group of nurses not having knee crepitus. Knee crepitus is often described as a grinding noise with a clearly palpable vibration, which could indicate cartilage damage. It is one of the signs for diagnosis of both Tibio-Femoral Joint (TFJ) and Patello-Femoral Joint (PFJ) OA, as described in the European league against rheumatism (EULAR) recommendation for diagnosis of knee OA [30].

The knee crepitus is considered as a sign of knee OA. This might indicate the presence of a relation between knee OA and high level of urinary CTXI-II biomarker. This finding suggests that CTX-II has a value in diagnosing early osteoarthritis.

4. CONCLUSION

In conclusion, in the present study there is high prevalence of occupational musculoskeletal disorders among operating room nurses. Future study on larger population in comparison to general population is recommended. Risk assessment of working conditions revealed multiple work related psychosocial, organizational and physical risk factors. The urinary biomarker CTX-II is suggested to have a value in diagnosing early osteoarthritis among OR nurses, but further research is required.

REFERENCES

1. Tinubu BMS, Mbada CE, Oyeyemi AL, Fabunmi AA. Work-related musculoskeletal disorders among nurses in Ibadan, South-West Nigeria: A cross-sectional survey. BMC Musculoskelet Disord. 2010;11:12.

2. Sauter S, Hales T, Bernard B, Fine L, Petersen M, Putz-Anderson V, et al. Summary of two NIOSH field studies of musculoskeletal disorders and VDT work among telecommunications and newspaper workers. Luczak H, Cakir A, Cakir G, editors. Elsevier Science Publishers, B.V.; 1993.

3. Shikdar AA, Al-Hadhrami MA. Operator performance and satisfaction in an ergonomically designed assembly workstation. Journal of Engineering Research. 2005;2(1):69-76.

4. Meijsen P, Knibbe HJ. Prolonged standing in the OR: A Dutch research study. AORN J. 2007;86(3):399-414.

5. Poole AR. Biochemical/immunochemical biomarkers of osteoarthritis: Utility for prediction of incident or progressive osteoarthritis. Rheumatic diseases clinics of North America. 2003;29:803-18.

6. Christgau S, Garner P, Fledeelius C, Moniz C, Ensig M, Gineys E, et al. Collagen Type II C-telopeptide fragments as an index of cartilage degradation. Bone. 2001;29(3):209-15.

7. Kuorinka I, Jonsson B, Kilbom A, et al. Standardized nordic questionnaires for the analysis of musculoskeletal symptoms. Appl Ergon. 1987;18:233-7.

8. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job Content Questionnaire (JCQ): An instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychology. 1998;3:322-55.

9. David G, Woods V, Li G, Buckle P. Further development of the usability and validity of the quick exposure check. Research Report: RR211/2005 Sudbury, Suffolk: HSE Books; 2005.

10. Murofuse NT, Marziale MHP. Diseases of the osteomuscular system in nursing workers. Rev. Latino-Am. Enfermagem. 2005;13(3):364-73.
11. Caruso CC, Waters R. A review of work schedule issues and musculoskeletal disorders with an emphasis on the healthcare sector. Ind Health. 2008; 46:523–34.

12. Sembajwe G, Tveito TH, Hopcia K, Kenwood C, O’Day ET, Stoddard AM, et al. Psychosocial stress and multi-site musculoskeletal pain: A cross-sectional survey of patient care workers. Workplace Health & Safety. 2013;61(3):117-25.

13. Garnero P, Rousseau JC, Delmas PD. Molecular basis and clinical use of biochemical markers of bone, cartilage, and synovium in joint disease. Arthritis Rheum. 2000;43:953–68.

14. Garnero P, Piperno M, Gineyts E, Christgau S, Delmas PD, Vignon E. Cross-sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: Relations with disease activity and joint damage. Ann Rheum Dis. 2001;60:619–626.

15. Vignon E, Garnero P, Delmas P, Avouac B, Bettica P, Boers M. Recommendations for the registration of drugs used in the treatment of osteoarthritis: An update on biochemical markers. Osteoarthritis Cartilage. 2001;9:289–93.

16. Kraus VB, Burnett B, Coindreau J, Cottrell S, Eyre D, Gendreau M, et al. Application of biomarkers in the development of drugs intended for the treatment of osteoarthritis. Osteoarthritis Cartilage. 2011;19(5):515–42.

17. Osbone D, Woodhouse S, Meacock R. Early changes in the sulfation of chondroitin in guinea-pig articular cartilage, a possible predictor of osteoarthritis. Osteoarthritis Cartilage. 1994;2(3):215–23.

18. Huebner JL, Hanes MA, Beekman B, TeKoppele JM, Kraus VB. A comparative analysis of bone and cartilage metabolism in two strains of guinea-pig with varying degrees of naturally occurring osteoarthritis. Osteoarthritis Cartilage. 2002;10(10):758-67.

19. Loeser RF. Age-related changes in the musculoskeletal system and the development of osteoarthritis. Clin Geriat Med. 2010;26(3):371-86.

20. Majachungiu G, Roy LS, Singh AJ, Florence L, Ningshen K. Correlation of urinary type-II collagen C telopeptide (Ctx-II) level with physical parameters among knee osteoarthritic patients. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2014;13(12):45-50.

21. Jung M, Christgau S, Lukoschek M, Henriksen D, Richter W. Increased urinary concentration of collagen type II C-telopeptide fragments in patients with osteoarthritis. Pathobiology. 2004;71(2):70-6.

22. Klussmann A, Gebhardt H, Liebers F, Engelhardt LV, David A, Bouillon B, et al. Individual and occupational risk factors for knee osteoarthritis – Study protocol of a case control study. BMC Musculoskeletal Disorders. 2008;9:26.

23. World Health Organization (WHO). Preventing musculoskeletal disorders in the workplace. Risk factor information and preventive measures for employers, supervisors and occupational health trainers. Protecting Workers Health Series no 5; 2003.

24. Buckwalter JA, Martin JA. Osteoarthritis. Adv Drug Deliv Rev. 2006;58:150-67.

25. Harma et al. The relation of age to the adjustment of the circadian rhythms of oral temperature and sleepiness to shift work. Chronobiology International. 1991;7:227-33.

26. Mouritzen U, Christgau S, Lehmann HJ, Tanko LB, Christiansen C. Cartilage turnover assessed with a newly developed assay measuring collagen type II degradation products: Influence of age, sex, menopause, hormone replacement therapy, and body mass index. Ann Rheum Dis. 2003;62:332-6.

27. Garnero P, Piperno M, Gineyts E, Christgau S, Delmas PD, Vignon E. Cross-sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: Relations with disease activity and joint damage. Ann Rheum Dis. 2001;60:619–26.

28. Saxton J. A review of current literature on physiological tests and soft tissue biomarkers applicable to work-related upper limb disorders. Occup Med (Lond). 2000;50:1.

29. Garnero P, Ayral X, Rousseau J, Christgau S, Sandell LJ, Dougados M, Delmas PD. Uncoupling of type II collagen synthesis and degradation predicts progression of
joint damage in patients with knee osteoarthritis. Arthritis & Rheumatism. 2002;46:2613–24.

30. Zhang W, Doherty M, Peat G, Bierma-Zeinstra MA, Arden NK, Bresnihan B, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. Ann Rheum Dis. 2010;69:483-9.