A cross-sectional study on serum high-sensitivity C-reactive protein level and shift work among reproductive age women

Abstract

Background: Among the inflammatory factors, high-sensitivity C-reactive protein (hs-CRP) is one of the strongest predictors of cardiovascular disease. This study aimed to evaluate the relationship of serum hs-CRP level with shift work among reproductive age women.

Methods: This cross-sectional study was conducted from September 2017 to May 2018 in three cities in Mazandaran Province, North of Iran. Through purposive sampling, 350 women (172 shift workers and 178 day workers) were recruited. The guideline recommended by the American Heart Association and the Centers for Disease Control and Prevention was used to interpret the result of hs-CRP measurement as the following: less than 1 µg/ml: low CVD risk; 1–3 µg/ml: moderate CVD risk; and more than 3 µg/ml: high CVD risk. The data were analyzed using the independent-sample t and the chi-square tests as well as the logistic regression analysis.

Results: 11.1% of participants had a serum hs-CRP level of more than 3 µg/ml. This rate among shift workers was significantly greater than day workers (15.6% vs. 7.0%; p=0.012). After adjusting the effects of potential confounders shift work significantly increased the odds of serum hs-CRP level of more than 3 µg/ml by 2.45 times (OR=2.45, 95% CI: 1.01–5.93, p=0.047).

Conclusion: Shift work is a significant predictor of high serum hs-CRP level probably due to its association with sleep problems and occupational stress. Improving the knowledge of female shift workers about the importance of quality sleep can reduce their CVD risk and improve their health.

Keywords: Shift work, Reproductive age, High-sensitivity C-Reactive Protein, Cardiovascular disease, Women

C-reactive protein (CRP) is a typical acute phase protein, which has increased in response to injury as well as systemic inflammation (1). CRP is a marker for infection and synthesized mainly by liver in response to proinflammatory cytokines (i.e. interleukin (IL)-1, IL-6, IL-17 and tumor necrosis factor-α) (2). High-sensitivity assay technique can detect CRP with a range of 0.01 to 10 mg/ l (3). hs-CRP is the most sensitive inflammatory marker and the strongest predictor of cardiovascular disease (CVD) (4, 5). Increases in serum hs-CRP level increase the risk of CVD by 2–5 times (4), diabetes mellitus (3), hypertension (6), depression (7) and cancer (8). Some studies have shown serum hs-CRP increases in shift workers (9, 10). Shift work is defined as the work in unusual work hours, i.e. at the time interval between 18:00 and 07:00.
The exact mechanism of greater risk of hs-CRP among shift workers is still unknown. Moreover, staying awake overnight causes disturbances in circadian rhythm and sleep-wake cycle (11). Circadian rhythm disturbances are associated with increase in the levels of proinflammatory cytokines (11) such as interleukin-1, interleukin-6 and tumor necrosis factor alpha (12). Interleukin-1 and interleukin-6 are the most significant factors behind the production of hs-CRP in the liver (13). Increases in the level of tumor necrosis factor alpha are also associated with increases in the level of serum hs-CRP (14).

Previous studies into the relationship of shift work and serum hs-CRP level reported contradictory results. For instance, a study among the workers of a coca processing company in Ghana found that serum hs-CRP level among shift workers was significantly higher than day workers (9). Two other studies among 1877 Finish airline-company employees and 96 Iraqi nurses also reported the same finding (10, 15). However, studies on Japanese workers and Iranian female shift work nurses found that shift work was not an independent significant predictor of serum hs-CRP level (13, 16). Their contradictory results may be related to work schedule, monthly night work (17), occupational stress (18) and gender (19).

Besides their contradictory results, most previous studies in this area were conducted on men, some certain occupational groups, and workers with different age, and no study had yet been conducted on reproductive women. Increase hs-CRP and related consequences among reproductive women is very important, because it has negative effects on reproduction, pregnancy, delivery, and fetal health and development (20). Thus, the present study was undertaken to fill this gap. This study will identify health problems of women in reproductive age; and it could be useful for planning prevention strategies in these employee women. Thus, the present study was undertaken to fill this gap. The aim of the study was to evaluate the relationship of serum hs-CRP level with shift work among reproductive age women.

Methods
Design: This two-group cross-sectional correlational study was conducted from September 2017 to May 2018 in the three cities of Amol, Babol, and Qhaemshahr, in Mazandaran Province, North of Iran. Study population:

Participants were female shift workers and day workers who were purposively selected from hospitals affiliated to Babol University of Medical Sciences, Babol, Iran, nursing homes, rehabilitation centers, and textile and sewing mills. Selection criteria were an age of 20–45, to be married, work experience of two years or more, no history of using contraceptive or estrogenic agents, no history of rheumatic disorders or infectious diseases in the past one week, no history of CVD, and a self-reported blood pressure of less than 140/90 at the beginning of employment. Participants were excluded if they voluntarily withdrew from the study. The sample size was calculated based on the results of an earlier study (15) the association between shift work and hs-CRP level which reported the difference between means score of hs-CRP in shift work and day work 0.3, and variance (1.8) \(^2\) (hs-CRP in the direction for shift work). Accordingly, with a confidence interval level of 95%, a power test of 80%, and a standardized effect size of 15% sample size was estimated to be 326, and considering probable withdrawal from the study, 350 female workers were recruited.

Data collection: Besides serum hs-CRP level, we assessed participants’ anthropometric indices as well as their conventional cardiovascular risk factors such as hypertension, hyperlipidemia, and diabetes mellitus in order to provide more reliable data about the effects of shift work on serum hs-CRP level.

Biomarkers assessment: In order to measure the serum levels of hs-CRP, triglyceride, high-density lipoprotein (HDL) and fasting blood sugar (FBS), a five-millilitre blood sample was obtained from each participant at 07:00–09:00 after a fasting period of 12–14 hours. Blood sampling was performed by the first author. Serum level of hs-CRP was measured using an enzyme-linked immunosorbent assay kit (Monobind Inc., USA) and a Hyperion ELISA reader device (USA). Moreover, HDL, triglyceride, and FBS levels were measured using Pars Azmoon kits (Pars Azmoon Inc., Tehran, Iran) and a biochemistry analyzer (Microsoft S800, Ireland). All laboratory tests were performed by one laboratory technician and in a hospital laboratory affiliated to Babol University of Medical Sciences, Babol, Iran. According to the guideline recommended by the American Heart Association and the Center for Disease Control and Prevention, the results of hs-CRP measurement were categorized as follows: less than 1 µg/ml: low CVD risk; 1–3 µg/ml: moderate CVD risk; and more than 3 µg/ml: high.
CVD risk (21). Moreover, triglyceride levels of more than 150 mg/dL, FBS levels of more than 110 mg/dl, and HDL levels of less than 40 mg/dL were considered abnormal (22).

**Anthropometric assessment:** Participants’ weight and height were measured at the upright position with no shoes and with minimum possible clothing covering the whole body. Weight and height measurements were done using an analogue weight scale (MW84, EmsiG Co., Gm-bH) and a wall-mounted plastic tape, respectively. Then, body mass index (BMI) was calculated and interpreted as the following: 18.5–25: normal; 25–30: overweight; and more than 30: obese. Waist circumference was also measured at the midway between the lowest rib edge and the iliac crest using a plastic tape. Anthropometric assessment was done by the first author.

**Blood pressure measurement:** An analogue sphygmomanometer (EmsiG Co., Gm-bH) was used to measure blood pressure from the right arm and after a fifteen-minute rest in the sitting position. A systolic blood pressure of more than 140 mm Hg or a diastolic blood pressure of more than 90 mm Hg was considered as hypertension. Participants who were taking antihypertensive medications were also classified as hypertensive (23). Blood pressure was measured by the first author.

**Shift work assessment:** Participants’ work schedule was classified as either shift work or day work. Those participants who did morning or evening work shifts or both and did less than five night shifts per month were classified as day workers, while those who did at least five night shifts per month were classified as shift workers.

**Assessment of demographic, occupational, and medical characteristics:** A questionnaire was used to assess participants’ demographic, occupational, and medical characteristics. The items of this questionnaire were on age, educational level, place of residence, family income level, number of children, work experience, monthly work hours, organizational position, workload, occupational stress, and CVD affliction. Workload and occupational stress were separately assessed using a question with a five-point Likert scale, the possible points of which ranged from “Light” to “Heavy” and from “Very low” to “Very high”, respectively. The history of CVD was also assessed through a self-report yes/no question.

**Assessment of health-related behaviors:** On cigarette smoking and alcohol consumption, each was assessed via a yes/no question. Sleep quality was also assessed via a question about the average sleep hours per day (responded as “Less than six hours” or “More than six hours”), a yes/no question about hypnotic use, a yes/no question about sleep adequacy, and a question about insomnia (responded on a four-point Likert scale as either “Never”, “Rarely”, “Often”, or “Always”). For physical activity assessment, participants who did thirty-minute physical activity at least thrice weekly were classified as physically active and those with lower levels of physical activity were classified as physically inactive.

**Statistical data analysis:** Data were analyzed via the SPSS for Windows program (v. 16.0. Chicago, IL, USA). The independent-sample t and the chi-square tests were performed to compare shift workers and day workers respecting their demographic, occupational, and medical characteristics and health-related behaviors. Moreover, the logistic regression analysis was employed to assess the effects of shift work on the odds of high serum hs-CRP level adjusted for potential confounders. The level of significance was set at less than 0.05.

**Ethical considerations:** The Ethics Committee of Babol University of Medical Sciences, Babol, Iran, approved this study (code: MUBABOL.HRI.REC.1395.58). Participants were granted the right to voluntarily withdraw from the study and then, their personal written informed consents were gotten.

**Results**

Participants’ demographic, occupational, and medical characteristics and health-related behaviors

Among the 350 participating female workers, twelve shift workers and six day workers were excluded due to voluntary withdrawal, reluctance to give a blood sample, incomplete answering to the study questionnaire, or inaccessibility during the study. Consequently, final data analysis was conducted on the data collected from 332 participants, i.e. 160 shift workers and 172 day workers. There were no statistically significant differences between participants and those who were excluded with respect to their demographic, occupational, and medical characteristics and health-related behaviors (p>0.05).

The means of participants’ age and work experience were 36.19±5.19 and 12.27±5.77 years, respectively. More than two thirds of them had university degrees (71%) and lived in urban areas (83%) and around two thirds of them were...
Serum high-sensitivity C-reactive protein level and shift work

healthcare providers (64%). There were no significant differences between shift workers and day workers with respect to their age, work experience, educational level, and employment status (p>0.05; table 1). More than half of the participants had heavy or very heavy workload, (61.9%) experienced high occupational stress (52.6%), and 11.8% of them suffered from CVD. Occupational stress and CVD rate among shift workers were significantly higher than day workers (p<0.01; table 1). Almost half of the participants reported sleep inadequacy (47.6%) and most of them reported sleeping more than six hours a day (84.8%). Shift workers reported significantly greater sleep inadequacy and lower sleeping hours a day than day workers (p<0.05; table 2).

Table1. Participants’ demographic, occupational, and medical characteristics

| Characteristics                  | Total                      | Group                      | P value |
|----------------------------------|----------------------------|----------------------------|---------|
| Age (Year) (Mean±SD)             | 36.19±5.29                 | 36.37±5.47                 | 0.52 a  |
| Work experience (Year) (Mean±SD) | 12.27±5.77                 | 11.74±5.27                 | 0.22 a  |
| Monthly work hours (Mean±SD)     | 185.90±22.21               | 192.61±23.33               | <0.001 a|
|                                  | 20–29                      | 35                         | 10.6    | 16 (9.4) |
|                                  | 30–39                      | 196                        | 59.4    | 87 (54.4)| 109 (64.1)| 0.19 b  |
|                                  | 40–45                      | 99                         | 30      | 54 (33.8)| 45 (26.5) |
| Educational level                |                            |                            |         |         |
| Bachelor’s                       | 234                        | 70.9                       | 112 (70.9)| 122 (70.9)|         |         |
| Diploma                          | 51                         | 15.5                       | 25 (15.8)| 26 (15.1)|         | 0.97 b  |
| Below diploma                    | 45                         | 13.6                       | 21 (13.3)| 24 (14)  |         |         |
| Place of residence               |                            |                            |         |         |
| Urban areas                      | 55                         | 16.7                       | 30 (19.0)| 25 (14.5)|         | 0.27 b  |
| Rural areas                      | 275                        | 83.3                       | 128 (81.0)| 147 (85.0)|         |         |
| Family income                    |                            |                            |         |         |
| Sufficient                       | 123                        | 37.20                      | 48 (30.4)| 71 (43.9)|         |         |
| Moderately sufficient            | 152                        | 46.2                       | 79 (50.0)| 73 (42.7)|         | 0.032 b |
| Insufficient                     | 54                         | 16.41                      | 31 (19.6)| 23 (13.5)|         |         |
| Physical activity                |                            |                            |         |         |
| Active                           | 143                        | 38.3                       | 61 (33.3)| 82 (43.2)|         | 0.51 b  |
| Inactive                         | 230                        | 61.7                       | 122 (66.7)| 108 (56.8)|         |         |
| Cigarette smoking                |                            |                            |         |         |
| Yes                              | 4                          | 1.2                        | 158      | 170      | 0.92 c  |
| No                               | 328                        | 98.81                      | 2 (1.2)  | 2 (1.2)  |
| Employment status                |                            |                            |         |         |
| Healthcare provider              | 273                        | 70.7                       | 136 (69.4)| 137 (72.1)|         |         |
| Mother aid or nurse aid          | 61                         | 15.7                       | 38 (19.4)| 23 (12.1)|         | 0.17 b  |
| Laborer                          | 34                         | 8.8                        | 15 (7.7) | 19 (10.0)|         |         |
| Service staff                    | 18                         | 4.7                        | 7 (3.6)  | 11 (5.8) |         |         |
| Workload                         |                            |                            |         |         |
| Light to moderate                | 123                        | 38.1                       | 51 (33.9)| 72 (42.9)|         |         |
| Heavy                            | 135                        | 41.8                       | 68 (43.9)| 67 (39.9)| 0.14 b  |
| Very heavy                       | 65                         | 20.1                       | 36 (23.2)| 29 (17.3)|         |         |
| Occupational stress              |                            |                            |         |         |
| Low                              | 38                         | 11.7                       | 18 (11.5)| 20 (11.8)|         |         |
| Moderate                         | 116                        | 35.7                       | 74 (43.8)| 74 (43.8)| 0.004 b |
| High                             | 171                        | 52.6                       | 96 (61.5)| 75 (44.4)|         |         |
| Cardiovascular problem           |                            |                            |         |         |
| Yes                              | 38                         | 11.8                       | 24 (15.6)| 14 (8.3) | 0.042 b |
| No                               | 285                        | 88.2                       | 130 (88.2)| 155 (91.7)|         |         |

a: The results of the independent-sample t test; b: The results of the Chi-square test; c: The results of the Fisher’s exact test
Table 2. Participants’ anthropometric indices, biomarkers, and sleep-related parameters

| Variables                          | Total | Group                  | P value |
|------------------------------------|-------|------------------------|---------|
|                                    | N     | Shift workers | Day workers |         |
|                                     | N (%) | N (%)       | N (%)      |         |
| Insomnia                           |       |              |            |         |
| Rarely                             | 152   | 47.5         | 57 (37.3)  | 95 (56.9)| 0.002 a|
| Mostly                             | 118   | 36.9         | 66 (43.1)  | 52 (31.1)|         |
| Always                             | 50    | 15.6         | 30 (19.6)  | 20 (12)  |         |
| Hypnotic use                       |       |              |            |         |
| Yes                                | 46    | 14.3         | 21 (13.7)  | 25 (14.9)| 0.76 a  |
| No                                 | 275   | 85.7         | 132 (86.3) | 143 (85.7)|         |
| Adequacy of sleep                  |       |              |            |         |
| Yes                                | 167   | 52.4         | 71 (46.4)  | 96 (57.8)| 0.041 a |
| No                                 | 152   | 47.6         | 82 (53.6)  | 70 (42.2)|         |
| Average daily sleep hours          |       |              |            |         |
| ≤ 6                                | 41    | 15.2         | 32 (23.7)  | 9 (6.7)  | 0.012 a |
| > 6                                | 228   | 84.8         | 103 (76.3) | 125 (93.3)|         |
| Body Mass Index (kg/m²)            |       |              |            |         |
| 18.5–25                            | 114   | 34.3         | 49 (30.6)  | 65 (37.8)|         |
| 25–30                              | 145   | 43.7         | 80 (50.0)  | 65 (37.8)|         |
| > 30                               | 73    | 22.0         | 31 (19.4)  | 24 (24.4)|         |
| Waist circumference (cm)           |       |              |            |         |
| < 88                               | 102   | 30.7         | 46 (28.8)  | 56 (32.6)| 0.45 a  |
| ≥ 88                               | 230   | 69.3         | 114 (71.3) | 116 (67.4)|         |
| Blood pressure (mm Hg)             |       |              |            |         |
| < 140/90                           | 324   | 97.6         | 155 (96.9) | 169 (98.3)| 0.48 b  |
| ≥ 140/90                           | 8     | 2.4          | 5 (3.1)    | 3 (1.7)  |         |
| Fasting blood sugar (mg/dL)        |       |              |            |         |
| < 110                              | 328   | 98.8         | 157 (98.1) | 171 (99.4)|         |
| ≥ 110                              | 4     | 1.2          | 3 (1.9)    | 1 (0.6)  | 0.35 a  |
| High-density lipoprotein (mg/dL)   |       |              |            |         |
| 50<                                | 266   | 19.9         | 137(85.6)  | 129(75.0)| 0.015 a |
| ≥ 50                               | 66    | 80.1         | 23(14.4)   | 43(25.0) |         |
| Triglyceride (mg/dL)               |       |              |            |         |
| < 150                              | 274   | 82.5         | 131 (81.9) | 143 (83.1)| 0.76 a  |
| ≥ 150                              | 58    | 17.5         | 29 (18.1)  | 29 (16.9)|         |
| hs-CRP μg/ml                        |       |              |            |         |
| ≤ 3 (Low and Moderate risk)        | 295   | 88.9         | 135 (84.4) | 160 (93.0)| 0.012 a |
| > 3 (High risk)                    | 37    | 11.1         | 25 (15.6)  | 12 (7.0) |         |

a: The results of the Chi-square test; b: The results of the Fisher’s exact test

Participants’ hs-CRP, biomarkers, and blood pressure:
The total mean of serum hs-CRP level was 1.27±1.57 µg/ml. This value among shift workers and day workers was respectively 1.45±1.80 and 1.11±1.32, with a statistically significant between-group difference (p=0.05). Moreover, 11.1% of participants had a serum hs-CRP level of more than 3 µg/ml. This rate was 15.6% among shift workers and 7.0% among day workers, with a significant between-group difference (p=0.012; table 2). Only 2.4% of participants suffered from hypertension and respectively 1.2%, 17.5%, and 63.6% of them had abnormal serum levels of FBS, triglyceride, and HDL. The between-group differences respecting hypertension rate and serum levels of FBS, triglyceride, and HDL were not statistically significant (p>0.05; table 2). The relationship of serum hs-CRP level with shift work The results of the logistic regression analysis illustrated that after adjusting the effects of the potential confounders (namely age, educational level, BMI, physical activity, occupational stress, work experience, work hours, and employment status), shift work significantly increased the risk of high hs-CRP by 2.45 times (OR=2.45, 95% CI: 1.01–5.93, p=0.047; table 3).
Moreover, 70% of our participants had university alignment eased the rate of high significant relationship of that shift work was not a significant factor behind hs nurses and Heydarikhayat et al. confirmed this result Korea than day workers. Several studies in Finland hs (31) level positively correlates with cigarette smoking hyperglycemia among study participants. Serum hs the lower rates of hypertension, cigarette smoking, and rate of high serum hs development awareness. Higher educational level is associated with greater (27, 28) Studies showed that serum hs CRP level based on different ages including women over 45. However, several other studies reported much higher rates of high serum hs-CRP level. For instance, this rate was 20.9% and 33.3% among Iranian women (16, 25) and 48% among American women who aged more than 45 (26). The lower rate of high serum hs-CRP level in the present study can be attributed to our participants’ age and educational level so that while an age of 20–45 was one of the selection criteria of the present study, those studies were conducted on women with different ages including women over 45. Studies showed that serum hs-CRP level increases with age (27, 28). Moreover, 70% of our participants had university degrees. Higher educational level is associated with greater awareness of CVD risk factors and hence, lower risk of CVD development (29). Another justification behind the lower rate of high serum hs-CRP level in the present study may be the lower rates of hypertension, cigarette smoking, and hyperglycemia among study participants. Serum hs-CRP level positively correlates with cigarette smoking rate (30, 31), blood pressure (23), and FBS level (32).

Study findings also showed that the rate of high serum hs-CRP level among shift workers was significantly greater than day workers. Several studies in Finland (11), Ghana (9), Korea (33), and Iraq (15) reported the same. Pavanello et al. and Heydarikhayat et al. confirmed this result (10, 34). However, two studies on Japanese workers (13) Omani nurses (35) and Netherlands health care workers (36) found that shift work was not a significant factor behind hs-CRP variations. One justification for the significant relationship of shift work with high serum hs-CRP level may be circadian misalignment due to shift work (37). A study which simulated the workplace of shift workers and day workers in a laboratory setting reported that circadian misalignment among shift workers significantly increased the rate of high serum hs-CRP level by 11% (37). Circadian misalignment increases the production of proinflammatory cytokines such as interleukin-1, interleukin-6 (12), and tumor necrosis factor alpha (12). Interleukin-1 and interleukin-6 are among the most significant factors behind the production of hs-CRP in the liver (13). Increases in the level of tumor necrosis factor alpha are also associated with increases in the level of serum hs-CRP (14).

Another justification for the significant relationship of shift work with high serum hs-CRP level may be the higher rate of sleep problems (such as insomnia and sleep inadequacy) among our shift worker participants. Some studies reported that sleep disturbances in shift workers is a factor risk to increase hs-CRP (17, 33), while, Puttonen et al. did not confirm these results (11). Sleep disturbances alter the expression of clock genes in the central and peripheral parts of the body clock center and thereby, increase inflammatory responses and serum levels of inflammatory factors such as hs-CRP(26). A study reported that the risk of high serum hs-CRP level among people with sleep duration of less than 5.5 hours a day was 2.2 times more than those with longer sleep duration (38).

The other justification for the higher serum level of hs-CRP among shift workers in our study may be the fact that their occupational stress was significantly greater than their day worker counterparts. Xu W et al. in their study among Chinese workers also showed that occupational stress
significantly increases risk of high hs-CRP 18). Previous studies showed that occupational stress among shift workers significantly increased serum cortisol level (39, 40). Through a complex process, cortisol stimulates the production of those cellular and molecular proteins which contribute to inflammation and thereby, increases the levels of inflammatory factors (41) such as hs-CRP. A study reported that through increasing inflammatory factors in vascular endothelium, both acute and chronic stress may induce atherosclerosis and result in CVD (42).

Limitations: This study was conducted using a cross-sectional design. Cohort studies are recommended to more carefully assessing the relationship of shift work with serum hs-CRP level. Moreover, rheumatic disorders among participants were assessed through the self-report method. Some participants might have been afflicted by these disorders but were unaware of such affliction. Therefore, future studies are recommended to screen participants respecting rheumatic disorders through clinical and laboratory methods.

In addition, study participants were reproductive women who worked as either shift workers or day workers. Assessment of unemployed and menopausal women can provide more reliable information about the effects of age and employment on serum hs-CRP level. The other study limitation was the small number of women who worked as laborer, mother aid, and nurse aid due to the small number of rehabilitation centers, nursing homes, and industrial mills with female workers in the study setting.

In conclusion, this study concludes that shift work is a significant predictor of high serum hs-CRP level among shift workers probably due to the higher prevalence of sleep problems and occupational stress among them. Strategies such as providing female shift workers with counseling services in order to improve their knowledge about the importance of quality sleep and healthy eating can reduce their serum hs-CRP level, improve their health status, and thereby, reduce CVD risk among them.

Acknowledgments

We would like to thank Ali Ghasemi, the technician of the laboratory of Beheshti Hospital, Babol, Iran, for helping us collect the study data and to all women participants in the study.

Funding: The present study was funded by the Health Research Institute in Babol University of Medical Sciences (grant no. 9542537).

Conflict of Interest: None declared.

References

1. Avan A, Tavakoly Sany SB, Ghayour-Mobarhan M, et al. Serum C-reactive protein in the prediction of cardiovascular diseases: Overview of the latest clinical studies and public health practice. J Cell Physiol 2018; 233: 8508-25.
2. Burke AP, Tracy RP, Kolodgie F, et al. Elevated C-reactive protein values and atherosclerosis in sudden coronary death: association with different pathologies. Circulation 2002; 105: 2019-23.
3. Kamath DY, Xavier D, Sigamani A, Pais P. High sensitivity C-reactive protein (hsCRP) & cardiovascular disease: an Indian perspective. Indian J Med Res 2015; 142: 261-8.
4. Czarkowska-Paczek B, Bartlomiejczyk I, Gabrys T, et al. Lack of relationship between interleukin-6 and CRP levels in healthy male athletes. Immunol Lett 2005; 99: 136-40.
5. Greiw AS, Gad Z, Mandil A, Wagdi M, Elneihoum A. Risk factors for cardiovascular diseases among school teachers In Benghazi, Libya. Ibnosina J Med Biomed Sci 2010; 2: 168-77.
6. Shafi Dar M, Pandith AA, Sameer AS, et al. hs-CRP: A potential marker for hypertension in Kashmiri population. Indian J Clin Biochem 2010; 25: 208-12.
7. Lee S, Oh SS, Jang SI, Park EC. Sex difference in the association between high-sensitivity c-reactive protein and depression: The 2016 Korea National Health and Nutrition Examination Survey. Sci Rep 2019; 9: 1918.
8. Lee S, Choe JW, Kim HK, Sung J. High-sensitivity C-reactive protein and cancer. J Epidemiol 2011: 21: 161-8.
9. Asare-Anane H, Abdul-Latif A, Ofori EK, Abdul-Rahman M, Amanquah SD. Shift work and the risk of cardiovascular disease among workers in cocoa processing company, Tema. BMC Res Notes 2015; 8: 798.
10. Heydarikhayat N, Mohammadinia N, Sharifipour H, Almasy A. Assessing frequency and causes of verbal abuse against the clinical staff. J Nurs Manag 2012; 1: 70-8.
11. Puttonen S, Viitasalo K, Härmä M. Effect of shiftwork on systemic markers of inflammation. Chronobiol Int 2011; 28: 528-35.
12. Prather AA, Marsland AL, Hall M, et al. Normative variation in self-reported sleep quality and sleep debt is associated with stimulated pro-inflammatory cytokine production. Biol Psychol 2009; 82: 12-7.
13. Amano H, Fukuda Y, Yokoo T, Yamaoka K. Interleukin-6 level among shift and night workers in Japan: Cross-sectional analysis of the J-HOPE study. J Atheroscler Thromb 2018; 25: 1206-14.
14. Giovannini S, Onder G, Liporoti R, et al. Interleukin-6, C-reactive protein, and tumor necrosis factor-alpha as predictors of mortality in frail, community-living elderly individuals. J Am Geriatr Soc 2011; 59: 1679-85.
15. Muhammad DH, Qadir FA. Effects of night shift working on some immunological, prostate specific antigen, cortisol level and malondialdehyde in male nurses at Hawler city. AIP Conference Proceedings 2017; 1888: id020035.
16. Naghashpour M, Amani R, Nematpour S, Haghighizadeh MH. Dietary, anthropometric, biochemical and psychiatric indices in shift work nurses. Food Nutr Sci 2013; 4: 1239-46.
17. Zheng H, Patel M, Hryniewicz K, Katz SD. Association of extended work shifts, vascular function, and inflammatory markers in internal medicine residents: a randomized crossover trial. JAMA 2006; 296: 1049-54.
18. Xu W, Chen B, Guo L, et al. High-sensitivity CRP: possible link between job stress and atherosclerosis. American J Ind Med 2015; 58: 773-9.
19. Lai MM, Li CI, Kardia SL, et al. Sex difference in the association of metabolic syndrome with high sensitivity C-reactive protein in a Taiwanese population. BMC Public Health 2010; 10: 429.
20. Dawson AJ, Krastev Y, Parsonage WA, et al. Experiences of women with cardiac disease in pregnancy: a systematic review and metasynthesis. BMJ Open 2018; 8: e022755.
21. Pfützner A, Forst T. High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diabetes Technol Ther 2006; 8: 28-36.
22. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001; 285: 2486.
23. Ebong IA, Schreiner P, Lewis CE, et al. The association between high sensitivity C-reactive protein and hypertension in women of the CARDIA study. Menopause 2016; 23: 662-8.
24. Hung J, Knuiman MW, Divitini ML, Davis T, Beilby JP. Prevalence and risk factor correlates of elevated C-reactive protein in an adult Australian population. Am J Cardiol 2008; 101: 193-8.
25. Tohidi M, Assadi M, Dehghani Z, et al. High sensitive C-reactive protein and ischemic heart disease, a population-based study. Iranian South Med J 2012; 15: 253-62.
26. Castanon-Cervantes O, Wu M, Ehlen JC, et al. Dysregulation of inflammatory responses by chronic circadian disruption. J Immunol 2010: 185: 5796-805.
27. Mohammed FM, Shafiq NA, Abdulhameed E. High sensitive C-reactive protein levels in pre and post menopausal healthy women in Kirkuk City-Iraq. Int J Vaccines Vaccin 2016; 2: 00021.
28. Woodard GA, Mehta VG, Mackey RH, et al. C-reactive protein is associated with aortic stiffness in a cohort of African American and white women transitioning through menopause. Menopause 2011; 18: 1291-7.
29. Hasan Lotfi M, Amiri F, Forouzannia SK, Fallahzadeh H. The association between socio-economic factors and coronary artery disease in Yazd province: a case-control study. J Comm Health Res 2014; 3: 168-76.
30. O'Loughlin J, Lambert M, Karp I, et al. Association between cigarette smoking and C-reactive protein in a representative, population-based sample of adolescents. Nicotine Tob Res 2008; 10: 525-32.
31. Van Dijk WD, Akkermans R, Heijdra Y, et al. The acute effect of cigarette smoking on the high-sensitivity CRP and fibrinogen biomarkers in chronic obstructive pulmonary disease patients. Biomarkers Med 2013; 7: 211-9.
32. Abdrabo AA. Association between fasting plasma glucose and highly sensitive C-reactive protein in a Sudanese population. Sudan Med J 2012; 48: 124-8.
33. Kim SW, Jang EC, Kwon SC, et al. Night shift work and inflammatory markers in male workers aged 20–39 in a display manufacturing company. Ann Occup Environ Med 2016; 28: 48.
34. Pavanello S, Stendardo M, Mastrangelo G, et al. Inflammatory long pentraxin 3 is associated with leukocyte telomere length in night-shift workers. Front Immunol 2017; 8: 516.

35. Akour A, Farha RA, Alefishat E, et al. Insulin resistance and levels of cardiovascular biomarkers in night-shift workers. Sleep Biol Rhythms 2017; 15: 283-90.

36. Loef B, van Baarle D, van der Beek AJ, et al. The association between exposure to different aspects of shift work and metabolic risk factors in health care workers, and the role of chronotype. PloS One 2019; 14: e0211557.

37. Morris CJ, Purvis TE, Mistretta J, Hu K, Scheer FA. Circadian misalignment increases C-reactive protein and blood pressure in chronic shift workers. J Biol Rhythms 2017; 32: 154-64.

38. Chiang JK. Short duration of sleep is associated with elevated high-sensitivity C-reactive protein level in Taiwanese adults: a cross-sectional study. J Clin Sleep Med 2014; 10: 743-9.

39. Nasir NM, Hashim Z. Work stress and cortisol level among shift workers in a tyre manufacturing factory in Selangor. Asia Pacific Environmen Occup Health J 2016; 2: 31-6.

40. Poantă L, Crăciun A, Dumitrașcu DL. Professional stress and inflammatory markers in physicians. Rom J Intern Med 2010; 48: 57-63.

41. Busillo JM, Cidlowski JA. The five Rs of glucocorticoid action during inflammation: ready, reinforce, repress, resolve, and restore. Trends Endocrinol Metab 2013; 24: 109-19.

42. Miller GE, Blackwell E. Turning up the heat: Inflammation as a mechanism linking chronic stress, depression, and heart disease. Curr Dir Psychol Sci 2006; 15: 269-72.