Research Article



Salivary cortisol concentrations in police officers – a cross-sectional study in Beijing, China

Yanxia Zhang¹, Jie Liu², Yanqing Liu³, Wei Lu⁴ and ⁽¹⁾ Ailian Hou⁵

¹Department of Public Health, Jining Psychiatric Hospital, Jining, China; ²Drug Rehabilitation Center, Jining Psychiatric Hospital, Jining, China; ³Department of General Practice, Jining No.1 People's Hospital, Jining, China; ⁴Department of Psychiatry, Huilongguan Hospital, Beijing, China; ⁵Department of Neurology, Fuling Central Hospital, Chongqing, China

Correspondence: Ailian Hou (pandafatt11@163.com)

Objective: We investigated the relationship between salivary cortisol level and the prevalence of depression 585 police officers working at the Police Departments of Beijing. Method: Cross-sectional data were obtained from 585 Chinese police officers recruited from Beijing, China. Salivary cortisol was assayed using the chemiluminescence immunoassay. A multiple logistic regression analysis adjusted for potential confounders was used to assess independent associations between salivary cortisol level and depression. Results: The median age of the included was 38 years (IQR, 29-45), 20.9% were female (n = 122). Finally, 15.6% (91/585; 95% CI: 12.6–18.5%) were considered to have depression. The median salivary cortisol level was significantly higher in police with depression than those police without depression [14.5(IQR, 11.9-15.9) nmol/l vs. 11.8(IQR, 9.4-14.2) nmol/l; P < 0.001]. The depression distribution across the salivary cortisol quartiles ranged between 5.4% (first quartile) and 26.9% (fourth quartile), P for trend <0.001. In multivariate models comparing the second (Q2), third and fourth quartiles against the first quartile of the salivary cortisol, cortisol in Q3 and Q4 were associated with depression, and increased prevalence of depression by 148% (OR: 2.48; 95% CI: 1.55-3.86) and 277% (3.77; 2.12-5.36). Based on ROC curves, the optimal cutoff value of salivary cortisol level to diagnose the depression was 13.8 nmol/l, which yielded the highest sensitivity and specificity [63.8% and 71.7%, respectively; area under the curve (AUC) = 0.695, 95% CI: 0.639-0.751; P < 0.0001]. Conclusions: The data showed that elevated levels of salivary cortisol were associated with increased prevalence of depression.

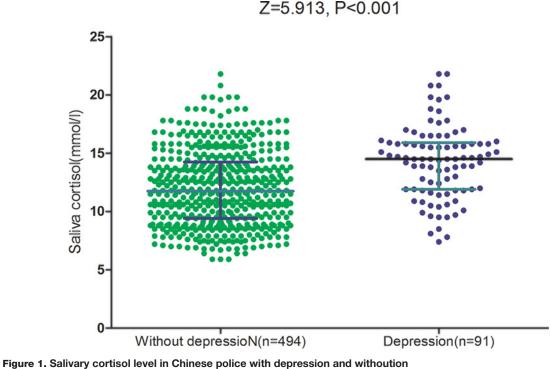
Introduction

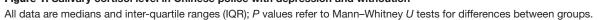
Previous studies have found that routine occupational stress or stressful work conditions have adverse effects on mental health [1]. Police officers are commonly considered to be a high-risk group for the development of mental health disturbances because of the various critical incidents and potential traumatic events they encounter during their career [2]. Previous studies had showed that work stress and trauma exposure may place police at heightened risk for the development of depression symptomatology [3]. Rates of major depression disorder and levels of depression symptoms were found to be higher in police than the general population and those with depression have poorer quality of life [4].

Violanti stated that policing was one of the most stressful jobs in U.S. society [5]. Work disability is related to poor quality of life and those with poorer quality of life are less likely to return to work [6]. Collins and Gibbs [7] pointed out that the proportion of police with measurable mental illness has doubled over the past 10 years. Another study showed that for each standard deviation increase in depressive symptoms, the prevalence ratio (PR) of suicide ideation increased 73 percent in police women (PR = 1.73, 95% CI = 1.32-2.27) and 67 percent in men (PR = 1.67, 95% CI = 1.21-2.30) [8]. Furthermore, the mental health problems among police officers can lead to anthropogenic and natural disasters [9]. Therefore,

Received: 05 December 2019 Revised: 15 March 2020 Accepted: 18 March 2020

Accepted Manuscript online: 26 March 2020 Version of Record published: 09 April 2020





rapidly measurable biomarkers to predict mental health are pivotal for optimized care and allocation of healthcare resources in police.

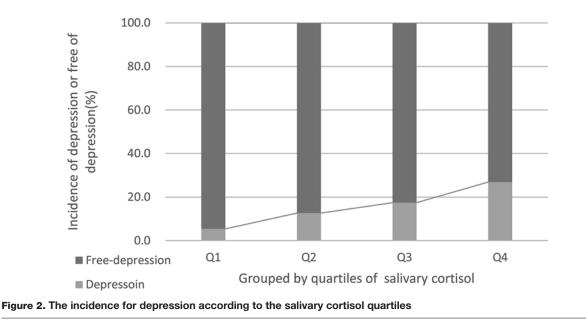
The major characteristic of the stress response is the activation of the sympathetic nervous system (SNS) and the hypothalamus–pituitary–adrenal (HPA) axis [10]. Any physical or psychological threat to homeostasis triggers release of corticotrophin-releasing hormone in the hypothalamus, and ultimately raises levels of steroid hormones such as cortisol in the blood stream and saliva [11]. Salivary cortisol is frequently used as a biomarker of psychological stress. Psychobiological mechanisms, which trigger the HPA axis can indirectly be assessed by salivary cortisol measures [12]. To date, assessment of cortisol in saliva is a widely accepted and frequently employed method. Due to several advantages over blood cortisol analyses (e.g. stress-free sampling, laboratory independence, lower costs), saliva cortisol assessment can be the method of choice in basic research and clinical environments [13].

The role of cortisol one the glucose, protein and fat metabolism, and cardiovascular reactivity had been proposed [14]. Cortisol hypersecretion is regarded as important in the pathophysiology of major depression, and depressed patients in the community appear to have increased early morning cortisol secretion [15]. Steudte-Schmiedgen et al. [16] found that major depression to be related to long-term attenuation in cortisol secretion. Interestingly, another study suggested that hair cortisol did predict depressive symptoms [17]. Thus, we speculated that level of salivary cortisol was associated with depressive symptoms in Chinese police officers. The aim of this descriptive and cross-sectional study was to investigate the relationship between salivary cortisol level and the prevalence of depression 585 police officers working at the Police Departments of Beijing.

Participants and methods Participants

Between October 2017 and December 2017, Chinese police officers working at the Police Departments of Beijing aged between 25 and 60 years were invited to participate in the study. The exclusion criteria were as following: (1) chronic diseases (e.g. hypertension, diabetes, liver and kidney disease); (2) disabling disease or reduced life expectancy (e.g. severe heart failure, severe respiratory, neurological or psychiatric illness, or late stages of cancer) or difficulty in communication; (3) using of possible or known cognition-impairing drugs in the previous 3-month; (4) inflammatory or infectious disease. Written informed consents were obtained after having provided verbal and written information





to participants. Ethics approval was granted by The Ethics Committee for Medical Research at the Fuling Central Hospital. All methods were performed in accordance with the relevant guidelines and regulations.

Clinical assessment

A validity assessed Self-Administered Questionnaire (SAQ) that was prepared in Chinese, was used to collect details pertaining to sociodemographic and occupational factors from the study participants. Sociodemographic details, including age, sex, race, body mass index (BMI), level of education (undergraduate and postgraduate), current smoker (yes vs. no) and marital status (Unmarried or divorced vs. married), location of residence (urban vs. rural), family yearly income (<200,000 vs. \geq 200,000), family problem [little time to spend with families, disharmony of marriage and child-upbringing problems] (yes vs. no), family history of mental illness (yes vs. no), lifestyle factors, self-care and use of medications were documented. Occupational information, including service experience (\leq 10 years vs. >10 years), infrastructure facilities (satisfactory vs. not satisfactory), welfare facilities (satisfactory vs. not satisfactory), working hours per week (>70 h vs. \leq 70 h), consecutive shift work per week (more frequently vs. less frequently), night shifts per month (>6 vs. \leq 6) and work satisfaction (satisfactory vs. not satisfactory) were recorded. Basic disease information was obtained from the latest year's medical report. To ensure the accuracy of the information collected, all demographic data were verified using the information in the household registry cards. Other information was based on self-report

Physical and depression measurement

Physical exercise was measured using the short version of the International Physical Activity Questionnaire (IPAQ), a self-reporting instrument that asks for an estimate of total weekly physical activity (walking/vigorous and moderate intensity activity) during the previous week. Physical activity levels were categorized into three (low, moderate, and high) categories following the scoring rule of IPAQ [18].

All participants were interviewed using the structured interview. The assessment and diagnostic instrument used in this survey was the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version (SCID-I/P) [19]. The SCID-I/P is a semi-structured diagnostic screening interview that covers 33 psychiatric disorders described in the fourth edition of the Diagnostic and Statistical Manual (DSM-IV) of the American Psychiatric Association (1994). Currently, it is widely used in diagnostic evaluation, clinical research, and in the training of mental health professionals in China and has been shown to be reliable and valid [20].

The diagnosis of depression was established using SCID through a one-stage screening process. The interviews were conducted by four mental health professionals. The interviewers' SCID diagnoses were compared with the expert-consensus diagnoses. Inter-rater reliability was examined in 45 participants and the kappa was 0.86. The severity of depressive symptoms was measured with the 17 item Hamilton depression rating scale (HAM-D) [21]. We have used the validated version for the Chinese population.



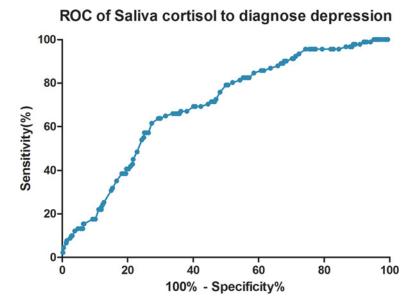


Figure 3. Receiver operator characteristic curve demonstrating sensitivity as a function of 1-specificity for predicting the depression based on the salivary cortisol level

Laboratory tests

The salivary samples were collected at 8:00 in the morning. The samples were quickly centrifuged to separate the supernatant from the cells and were then immediately frozen at -80° C until analysis. All analyses were performed in duplicate by the same researcher. Salivary cortisol was assayed using the chemiluminescence immunoassay (Elecsys Cortisol, Roche Diagnostics International AG, Rotkreuz, CH), according to manufacturer instructions. Intra- and inter- assay coefficients of variation were 4% and 6%, respectively. Salivary cortisol levels were expressed in nmol/l. Some of included (N = 75) collected salivary samples at 6 time-points: (1) on awakening; (2) at 8:00; (3) at 12:00; (4) at 15:00; (5) at 18:00 and (6) at 21:00. The participants were asked to collect the first (awakening) and the last (bed time) samples in a specific time window: Not later than 10:00 for the first and not later than midnight for the last sample.

Statistical analysis

The results are expressed as percentages for categorical variables and as median (interquartile range, IQR) for the continuous variables. Correlations among continuous variables were assessed by the spearman rank-correlation coefficient. Proportions were compared by the Chi-square test, and the Mann–Whitney test was used to compare continuous variables between groups.

The relation of salivary cortisol with depression was investigated with the use of logistic regression models. We used crude models and multivariate models and report odds ratios (ORs). ORs were also calculated according to equal quartiles of the distributions of salivary cortisol, and trends across these quartiles were tested by using conditional logistic regression models. For multivariate analysis, we included significant predictors as assessed in univariate analysis. For a more detailed exploration of the salivary cortisol and depression, we also used multivariate analysis models to estimate adjusted OR and 95% CIs of depression for salivary cortisol quartiles (with lowest quartile as reference). The influence of elevated levels of salivary cortisol (defined as more or equal to third quartile) on depression was also performed.

At last, receiver operating characteristic curves (ROC) was used to test the overall prognostic accuracy of the salivary cortisol and results were reported as area under the curve (AUC). All statistical analysis was performed with SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, U.S.A.). Statistical significance was defined as P < 0.05.

Results

After excluding 139 participants, 585 Chinese police were included in the study. The response rate of this survey was 80.8% (95% CI: 77.9–83.7%). The reasons for failing to participate included: 52 subjects refused to participate; 62 suffered from chronic diseases; 12 subjects lost samples; and 13 subjects were due to incomplete data. There were no



Table 1 Baseline characteristics according to depressive status

	ALL	Depression	Without depression	P [†]
Ν	585	91	494	-
Age (years, IQR)	38 (29–45)	44 (33–49)	39 (27–42)	0.015
Female, N (%)	122 (20.9)	32 (35.2)	90 (18.2)	<0.001
Ethnicity-Han, N (%)	533 (91.1)	82 (90.1)	451 (91.3)	0.715
BMI (m²/kg, IQR)	28.6 (25.4–30.3)	29.6 (26.8–31.7)	28.2 (25.0–29.6)	0.032
Education: Postgraduate or more, N (%)	211 (36.1)	35 (38.5)	176 (35.6)	0.605
Marital status: Unmarried or divorced, N (%)	133 (22.7)	23 (25.3)	110 (22.3)	0.529
Family problem, N (%)	178 (30.4)	36 (39.6)	142 (28.7)	0.039
Location of residence: urban, N (%)	422 (72.1)	64 (70.3)	358 (72.5)	0.676
Family yearly income: <200,000, N (%)	268 (45.8)	46 (50.5)	222 (44.9)	0.324
Current smoker, N (%)	189 (32.3)	33 (36.3)	156 (31.3)	0.380
Family history of mental illness, N (%)	65 (11.1)	18 (19.8)	47 (9.5)	0.004
Service experience: ≤ 10 years, N (%)	311 (53.2)	48 (52.7)	263 (53.2)	0.931
Infrastructure facilities: Satisfactory, N (%)	388 (66.3)	44 (48.4)	344 (69.6)	<0.001
Welfare facilities: Satisfactory, N (%)	331 (56.6)	41 (45.1)	290 (58.7)	0.016
Working hours per week: >70 h, N (%)	355 (60.7)	70 (76.9)	285 (57.7)	0.001
Consecutive shift work per week: More frequently, N (%)	303 (51.8)	68 (74.7)	235 (47.6)	<0.001
Night shifts per month: >6 , N (%)	269 (46.0)	55(60.4)	214(43.3)	0.003
Work satisfaction: Not satisfactory, N (%)	249 (42.6)	56(61.5)	193(39.1)	<0.001
Physical activity [‡]				0.009
Low	202 (34.5)	43(47.3)	159(32.2)	
Moderate	190 (32.5)	28(30.7)	162(33.8)	
High	193 (33.0)	20(22.0)	173(35.0)	

[†]Value was assessed using Mann–Whitney *U* test or Chi-Square test.

[‡]Physical activity levels were categorized into three (low, moderate, high) categories following the scoring rule of the IPAQ [21].

Data are presented as median (IQR) or number (%); IQR, interquartile range; BMI, body mass index; IPAQ, International Physical Activity Questionnaire

statistically significant differences in sex, age, or location of resident between the participants and non-participants. The median age of the included was 38 years (IQR, 29–45), 20.9% were female (n = 122), and median police rank duration was 8.0 (IQR: 4.0–15.0) years. The median HAM-D score was 5 (IQR, 3–10). Finally, 15.6% (91/585; 95% CI: 12.6–18.5%) were considered to have depression. Prevalence of depression was greater among women (35.2%) than men (18.2%). Among those patients with depression, only 6.6% (6/91) start to take psychotropic medications after the diagnosis. The baseline characteristics of those participants were described in Table 1.

As shown in the Table 1, police with depression were older and more frequently were female, obesity and unmarried or divorced. They were more frequently with family history of mental illness, consecutive shift work per week and night shifts per month. Furthermore, those people were also Less frequently with satisfactory welfare facilities, colleague support and work satisfaction. No association was found between duration of work and the presence of depression.

The data showed that the median salivary cortisol level was 12.1 (IQR, 9.6–14.7) nmol/l. The median salivary cortisol level was significantly higher in police with depression than those police without depression [14.5 (IQR, 11.9–15.9) nmol/l vs. 11.8 (IQR, 9.4–14.2) nmol/l; P < 0.001; Figure 1]. The higher salivary cortisol level corresponded to the higher HAM-D score (r = 0.615, P < 0.001). There was a modest correlation between levels of cortisol and age (r = 0.182, P = 0.015). There was no correlation between levels of cortisol and sex (P = 0.275) and BMI (P = 0.095).

The salivary cortisol level was the marker associated with the presence of depression (OR 1.24, 95% CI: 1.15–1.33; P < 0.001). Multivariate logistic regression analysis considering traditional risk factors showed a positive relationship between salivary cortisol level and depression when salivary cortisol level was used as a continuous variable (OR, 1.16; 95% CI, 1.07–1.24; P < 0.001; Table 2). In addition, sex, age, BMI, family history of psychiatric disorders, infrastructure facilities, working hours per week, consecutive shift work per week, night shifts per month, work satisfaction and physical activity were also associated with the presence of depression unlike other factors (Table 2).

The probability of depression increased gradually with increasing salivary cortisol quartiles (Figure 2). The depression distribution across the salivary cortisol quartiles ranged between 5.4% (first quartile) to 26.9% (fourth quartile),

Variable	OR (95% CI)	Р	
Age (>40 years vs. \leq 40 years)	1.53 (1.22–2.18)	0.036	
Sex (Female vs. male)	1.76 (1.28–2.11)	0.003	
BMI (>30 vs. ≤30 kg/m²)	1.44 (1.19–2.17)	0.041	
Family problem (Yes vs. no)	1.33 (0.95–2.04)	0.205	
Family history of mental illness (Yes vs. No)	1.68 (1.19–2.46)	0.009	
Infrastructure facilities (Satisfactory vs. Not satisfactory)	0.63 (0.42–0.88)	0.003	
Welfare facilities (Satisfactory vs. Not satisfactory)	0.84 (0.72–1.03)	0.059	
Working hours per week (>70 h vs. \leq 70 h)	1.83 (1.27–2.87)	0.011	
Consecutive shift work per week (More vs. Less frequently)	2.26 (1.42–3.31)	0.008	
Night shifts per month (>6 vs. ≤6)	1.39 (1.08–1.93)	0.027	
Work satisfaction (Not satisfactory vs. Satisfactory)	1.51 (1.28–1.88)	<0.001	
Physical activity (low vs. moderate + high)	2.42 (1.76–3.14)	<0.001	
Salivary cortisol (increase per unit)	1.16 (1.07–1.24)	<0.001	

Table 2 Multivariate logistic regression for depression in Chinese police (n = 585)[†]

[†]Adjusted for those significant risk factors that confirmed in the univariate analysis: sex, age, BMI, family history of psychiatric disorders, family problem, infrastructure facilities, welfare facilities, working hours per week, consecutive shift work per week, night shifts per month, work satisfaction, physical activity and salivary cortisol.

widowhood, living with offspring, years of education, and plasma levels of HCY, CRP, IL-6 and HCY.

OR = odds ratio; CI = confidence interval

Table 3 Multivariate logistic regression analysis for depression according to salivary cortisol quartiles

Salivary cortisol quartiles †	Depression/All	Crude OR (95% CI), P	Multivariable-adjusted [‡] , ${m P}^{\dagger\dagger}$
Q1	8/149	Reference	Reference
Q2	18/142	2.56 (1.08-6.09), 0.029	1.88 (0.93–3.55), 0.076
Q3	26/149	3.73 (1.63–8.53), 0.001	2.48 (1.55–3.86), 0.009
Q4	39/145	6.49 (2.91–14.45), <0.001	3.77 (2.12–5.36), <0.001
Elevated vs. normal	39/145 vs. 52/440	2.75 (1.72–4.38), <0.001	2.05 (1.38–3.06), 0.003

[†]Salivary cortisol in Quartile 1 (<9.6 nmol/l), Quartile 2 (9.6–12.1 nmol/l), Quartile 3 (12.1–14.7 nmol/l), and Quartile 4 (>14.7 nmol/l). Elevated salivary cortisol level was defined as more than the Q3 level (>14.7 nmol/l).

[‡]Adjusted for those significant risk factors that confirmed in the univariate analysis: sex, age, BMI, family history of psychiatric disorders, family problem, infrastructure facilities, welfare facilities, working hours per week, consecutive shift work per week, night shifts per month, work satisfaction, physical activity and salivary cortisol.

^{††}*P* value for the trend <0.001

Abrreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

P for trend <0.001. In multivariate models comparing the second (Q2), third and fourth quartiles against the first quartile of the salivary cortisol (Table 3), cortisol in Q3 and Q4 were associated with depression, and increased prevalence of depression by 148% (OR: 2.48; 95% CI: 1.55–3.86) and 277% (3.77; 2.12–5.36). The independent association of salivary cortisol with depression was confirmed using the likelihood ratio test (P < 0.001). In a multivariate model using the elevated levels of salivary cortisol (>Q3) versus normal together with the other significant variables, the marker displayed prognostic information (depression: OR for high salivary cortisol, 2.05 [95% CI, 1.38–3.06; P = 0.003]).

Based on ROC curves, the optimal cutoff value of salivary cortisol level to diagnose the depression was 13.8 nmol/l, which yielded the highest sensitivity and specificity [63.8% and 71.7%, respectively; area under the curve (AUC) = 0.695, 95% CI: 0.639–0.751; P < 0.0001; Figure 3]. Further, in our study, we found that an increased prevalence of depression was associated with salivary cortisol \geq 13.8 nmol/l (unadjusted OR 4.25, 95% CI: 2.67–6.78). This relationship was confirmed in the dose–response model. In multivariate analysis, there was an increased prevalence of depression associated with salivary cortisol \geq 13.8 nmol/l (OR 3.09, 95% CI: 1.64–4.77; P < 0.001) after adjusting for above possible confounders.

Salivary samples were obtained from six time-point in a subgroup of 75 police, 12 of whom subsequently experienced depression. The result showed the time course of salivary cortisol, showing significant changes with time of sampling (P < 0.001), with peak concentrations on awakening (P < 0.001, compared with other time-point), falling



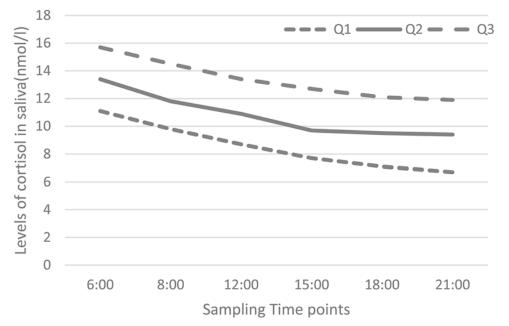
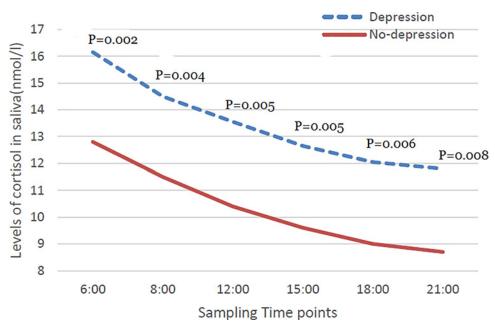
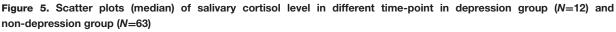


Figure 4. Scatter plots (median, interquartile ranges) of salivary cortisol level in different time-point (N = 75)





P values refer to Mann–Whitney *U* tests for differences between groups.

to a plateau by 15:00 to 21:00 (Figure 4). The Figure 5 also showed that same trend in depression and non-depression groups. Furthermore, the median salivary cortisol level was significantly higher in police with depression than those police without depression in all the six time-point (Figure 5).

Discussion

To the best of our knowledge, it is the first time to assess the relationship between salivary cortisol level and the prevalence of depression in Chinese police officers. Our main findings were as the following: (1) 15.6% of the police



officers were considered to have depression, and prevalence of depression was greater among women (35.2%) than men (18.2%); (2) The median salivary cortisol level was significantly higher in police with depression than those police without depression; (3) Elevated levels of salivary cortisol were associated with increased prevalence of depression and might be useful in identifying police officers at risk for depression for early prevention strategies.

In the present study, we found that the estimated rate of probable depression in police officers was 15.6%. The previous studies had reported that the prevalence of depression has a wide range from 21.6% among Taiwan police officers [4] to 65.6% among Australian police officers [22]. Wickramasinghe et al. [9] found that the estimated prevalence of depression in the police sample was 22.8% (95% CI 19.9–26.1%), and the adjusted prevalence of depression was 10.6% (95% CI 6.6–15.1%). We have a relatively low incidence. This might probably cause by the fact that people with chronic diseases has been ruled out. Furthermore, there were variations in sites of survey, sampling methods, screening instruments, diagnostic criteria, types of interviewer, culture, social and economic status between the various studies [23]. Those variations make it difficult to compare different studies.

Rates of major depression disorder and levels of depression symptoms were reported as higher among police officers than the general population [4]. Our study is also higher than the estimated rate of 2.0% for major depression in metropolitan China [24] and higher than that indicated in another study in four provinces (Shandong, Zhejiang, Qinghai and Gansu provinces) from 2001 to 2005 [25]. They reported the adjusted one-month prevalence of a major depressive episode was 1.55% and 2.60% for men and women, respectively. Another study found that the percent of officers with depression was nearly double (12.0% vs. 6.8%) and officers were nearly four times more likely to sleep less than 6 h in a 24-h period than the general population (33.0% vs. 8.0%) [26].

In the present study, we found that prevalence of depression was greater among women (35.2%) than men (18.2%). Similarly, two previous studies had showed that prevalence of depression was greater among women (22.0%) than men (12.1%) [27], and depressive symptoms were higher among women than men officers (12.5% vs. 6.2%) [8]. Women showed greater HPA axis activation than men and that menopause with loss of estrogens showed the greatest HPA axis dysregulation [28].

Cortisol is an HPA axis-related hormone with a robust circadian rhythm where levels typically peak in the morning hours and decline across the day [29]. In the present study, we also found that salivary cortisol was with peak concentrations on awakening and falling to a plateau at afternoon. In the present study, we found that elevated levels of salivary cortisol were associated with increased prevalence of depression. Police work is considered a stressful occupation that not only involves danger and traumatic event exposure, but also organizational stressors such as lack of administrative support, punishment centered executive philosophies and excessive paperwork [30]. The activity of the HPA axis may be dysregulated in this population lead to a high risk of depression [31,32]. Belanoff et al. [33] found that greater secretion of cortisol might be present in depressed subjects after clinical recovery and withdrawal of medication. A meta-analysis showed that elevated cortisol was associated with depression, with a stronger effect in older inpatients with melancholic or psychotic depression [34]. Furthermore, Grynderup et al. [35] found that a steeper cortisol slope over the day was protective for incident depression, and each 1.0 nmol/l increase in daily mean cortisol concentration was associated with a 47% reduction in depression risk, while each 1.0 nmol/l difference in morning and evening salivary cortisol concentration was associated with a 36% lower risk of depression.

The causal relationship between salivary cortisol and depression needs further study. A previous study demonstrated differential effects of burnout and perceived stress on HPA axis regulation [36]. Some other studies had showed that elevated levels of cortisol might play a role in pathophysiology of depression. One study concluded that in healthy adults elevated free cortisol levels are associated with impaired memory function [37]. Another study suggested that basal cortisol elevation may cause hippocampal damage and impair hippocampus-dependent learning and memory in humans [38]. Chronic exposure to high cortisol levels leads to structural and functional changes in various glucocorticoid receptor-rich brain regions fundamental for emotional and cognitive function, including the hippocampus, amygdala and prefrontal cortex [39]. At last, high cortisol was associated with altered neurotransmitter function, e.g. diminished brain serotonin synthesis, low CSF 5HIAA and increased noradrenergic activity [40]. Further prospective research is warranted.

Strengths and limitations

Salivary cortisol collection allows for non-invasive timed collection of free cortisol, which is stable for several days before processing, allowing for a valid assessment of the HPA axis in the free-living state [41]. The assessment of cortisol in saliva has proven a valid and reliable reflection of the respective unbound hormone in blood [13]. Thus, in the present study, we assess the levels of cortisol by the salivary samples. Furthermore, the salivary cortisol was



assayed using the chemiluminescence immunoassay with a higher sensitivity and specificity when compared with the enzyme-linked immunosorbent assay.

Some limitations of our study should be taken into account. First, because both salivary cortisol and current depression symptoms were assessed one time at the admission, it is difficult to determine a causal relationship. In addition, the applicability to the workplace may be limited in that salivary cortisol sampling, although non-invasive, may still be impractical or unlikely in the workplace. Second, since the response rate of this survey was 80.8%, 19.2% of eligible respondents were not represented in the sample. Third, the present study was lack of functional assessment of HPA axis in parallel and no information about salivary gene expression. Fourth, since the time of awakening is not reported in the manuscript, it is impossible to know whether the samples were collected within the influence of the cortisol awakening response (CAR). This may change drastically the results and the interpretation of the findings. Furthermore, we have to control for the time of awakening in the analyses. Finally, it is possible that the relatively low prevalence of depression symptoms in our sample may be due to a tendency to under-report due to concerns about employment status. In addition, some people with chronic diseases, who more likely suffered from depression has been ruled out. This potential response bias may impact the generalizability of our results.

Conclusions

The data showed that elevated levels of salivary cortisol were associated with increased prevalence of depression and might be useful in identifying police officers at risk for depression for early prevention strategies. The incidence of depression in police officers were not uncommon, suggesting that steps should be taken to prevent depression and improve the mental well-being of these workers.

Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

Funding

The authors declare that there are no sources of funding to be acknowledged.

Author Contribution

H.A. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Z.Y., L.J., Liu Y., H.A.; Acquisition of data: Z.Y., Liu J., Liu Y.; Analysis and interpretation of data: Lu Y., H.A.; Drafting of the manuscript: Z.Y., L.J., Liu Y., Lu Y.; Critical revision of the manuscript for important intellectual content: H.A.; Administrative, technical, or material support: Z.Y., L.J., Liu Y., Lu Y; Study supervision: H.A.

Abbreviations

AUC, area under the curve; BMI, body mass index; DSM, Diagnostic and Statistical Manual; HPA, hypothalamus–pituitary–adrenal; IPAQ, International Physical Activity Questionnaire; IQR, interquartile range; OR, odds ratio; PR, prevalence ratio; ROC, receiver operating characteristic curves; SAQ, self-administered questionnaire; SCID-I/P, Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version; SNS, sympathetic nervous system.

References

- 1 Liberman, A.M., Best, S.R., Meltzer, T.J., Fagan, J.A., Weiss, D.S. and Marmar, C.R. (2002) Routine occupational distress in police. *Policing: An Int. J. Police Strategies Manage.* **25**, 421–441, https://doi.org/10.1108/13639510210429446
- 2 van der Velden, P.G., Rademaker, A.R., Vermetten, E. et al. (2013) Police officers: a high-risk group for the development of mental health disturbances? A cohort study. *BMJ Open* **3**, e001720, https://doi.org/10.1136/bmjopen-2012-001720
- 3 Wang, Z., Inslicht, S.S., Metzler, T.J. et al. (2010) A prospective study of predictors of depression symptoms in police. *Psychiatry Res.* **175**, 211–216, https://doi.org/10.1016/j.psychres.2008.11.010
- 4 Chen, H.C., Chou, F.H.C., Chen, M.C. et al. (2006) A survey of quality of life and depression for police officers in Kaohsiung, Taiwan. *Qual. Life Res.* **15**, 925–932, https://doi.org/10.1007/s11136-005-4829-9
- 5 Violanti, J.M. (1992) Coping strategies among police recruits in a high-stress training environment. *J. Soc. Psychol.* **132**, 717–729, https://doi.org/10.1080/00224545.1992.9712102
- 6 Pattani, S., Constantinovici, N. and Williams, S. (2004) Predictors of reemployment and quality of life in NHS staff one year after early retirement because of ill health; a national prospective study. *Occup. Environ. Med.* **61**, 572–576, https://doi.org/10.1136/oem.2003.011817
- 7 Collins, P.A. and Gibbs, A.C. (2003) Stress in police officers: a study of the origins, prevalence and severity of stress-related symptoms within a county police force. Occup. Med. 53, 256–264, https://doi.org/10.1093/occmed/kqg061
- 8 Violanti, J.M., Fekedulegn, D., Charles, L.E. et al. (2009) Suicide in police work: Exploring potential contributing influences. *Am. J. Criminal Justice* **34**, 41–53, https://doi.org/10.1007/s12103-008-9049-8



- 9 Wickramasinghe, N.D., Wijesinghe, P.R., Dharmaratne, S.D. et al. (2016) The prevalence and associated factors of depression in policing: a cross sectional study in Sri Lanka. *Springer Plus* **5**, 1776, https://doi.org/10.1186/s40064-016-3474-9
- 10 McEwen, B.S. (2007) Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol. Rev.* 87, 873–904, https://doi.org/10.1152/physrev.00041.2006
- 11 Evans, K.D., Douglas, B., Bruce, N. et al. (2008) An exploratory study of changes in salivary cortisol, depression, and pain intensity after treatment for chronic pain. *Pain Med.* 9, 752–758, https://doi.org/10.1111/j.1526-4637.2006.00285.x
- 12 Hellhammer, D.H., Wüst, S. and Kudielka, B.M. (2009) Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology* **34**, 163–171, https://doi.org/10.1016/j.psyneuen.2008.10.026
- 13 Kirschbaum, C. and Hellhammer, D.H. (1994) Salivary cortisol in psychoneuroendocrine research: recent developments and applications. *Psychoneuroendocrinology* **19**, 313–333, https://doi.org/10.1016/0306-4530(94)90013-2
- 14 Zi, W.J. and Shuai, J. (2013) Cortisol as a prognostic marker of short-term outcome in Chinese patients with acute ischemic stroke. *PLoS ONE* **8**, e72758, https://doi.org/10.1371/journal.pone.0072758
- 15 Bhagwagar, Z., Hafizi, S. and Cowen, P.J. (2005) Increased salivary cortisol after waking in depression. *Psychopharmacology (Berl.)* **182**, 54–57, https://doi.org/10.1007/s00213-005-0062-z
- 16 Steudte-Schmiedgen, S., Wichmann, S., Stalder, T. et al. (2017) Hair cortisol concentrations and cortisol stress reactivity in generalized anxiety disorder, major depression and their comorbidity. J. Psychiatr. Res. 84, 184–190, https://doi.org/10.1016/j.jpsychires.2016.09.024
- 17 Mayer, S.E., Lopez-Duran, N.L., Sen, S. et al. (2018) Chronic stress, hair cortisol and depression: A prospective and longitudinal study of medical internship. *Psychoneuroendocrinology* **92**, 57–65, https://doi.org/10.1016/i.psyneuen.2018.03.020
- 18 Craig, C.L., Marshall, A.L., Sjöström, M. et al. (2003) International physical activity questionnaire: 12- country reliability and validity. *Med. Sci. Sports Exerc.* 35, 1381–1395, https://doi.org/10.1249/01.MSS.0000078924.61453.FB
- 19 Zhang, B., Li, T., Huang, Y. and Liu, X.H. (2007) *The Chinese version of Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version (SCID-I/P)*, Patient edition The Institute of Mental Health of West China Hospital, Sichuan University, Beijing, in Chinese
- 20 Phillips, M.R. and Liu, X.H. (2011) Translated and adapted Chinese version of Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version (SCID-I/P), Patient edition Suicide Research and Prevention Center, Shanghai Mental Health Center, Shanghai, In: First, Michael B., Spitzer, Robert L., Gibbon, Miriam, Williams, Janet B.W. (Eds.)
- 21 Hamilton, M. (1960) A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62, https://doi.org/10.1136/jnnp.23.1.56
- 22 Lawson, K.J., Rodwell, J.J. and Noblet, A.J. (2012) Mental health of a police force: estimating prevalence of work-related depression in Australia without a direct national measure. *Psychol. Rep.* **110**, 743–752, https://doi.org/10.2466/01.02.13.17.PR0.110.3.743-752
- 23 Guo, W.J., Tsang, A., Li, T. and Lee, S. (2011) Psychiatric epidemiological surveys in China 1960–2010: how real is the increase of mental disorders? *Curr. Opin. Psychiatry* **24**, 324–330, https://doi.org/10.1097/YC0.0b013e3283477b0e
- 24 Shen, Y.C., Zhang, M.Y., Huang, Y.Q., He, Y.L., Liu, Z.R., Cheng, H. et al. (2006) Twelve-month prevalence, severity, and unmet need for treatment of mental disorders in metropolitan China. *Psychol. Med.* 36, 257–267, https://doi.org/10.1017/S0033291705006367
- 25 Phillips, M.R., Zhang, J., Shi, Q., Song, Z., Ding, Z., Pang, S. et al. (2009) Prevalence, treatment, and associated disability of mental disorders in four provinces in China during 2001–05: an epidemiological survey. *Lancet* **373**, 2041–2053, https://doi.org/10.1016/S0140-6736(09)60660-7
- 26 Hartley, T.A., Burchfiel, C.M., Fekedulegn, D. et al. (2011) Health disparities in police officers: comparisons to the US general population. *Int. J. Emerg. Ment. Health* **13**, 211–220
- 27 Darensburg, T., Andrew, M.E., Hartley, T.A. et al. (2006) Gender and age differences in posttraumatic stress disorder and depression among Buffalo police officers. *Traumatology* 12, 220–228, https://doi.org/10.1177/1534765606296271
- 28 Young, E. and Korszun, A. (2010) Sex, trauma, stress hormones and depression. Mol. Psychiatry 15, 23–28, https://doi.org/10.1038/mp.2009.94
- 29 Flynn, M., Cicchetti, D. and Rogosch, F. (2014) The prospective contribution of childhood maltreatment to low self-worth, low relationship quality, and symptomatology across adolescence: A developmental-organizational perspective. *Dev. Psychol.* **50**, 2165, https://doi.org/10.1037/a0037162
- 30 Violanti, J.M., Charles, L.E., Gu, J.K. et al. (2013) Associations of depressive symptoms and brachial artery reactivity among police officers. Safety Health Work 4, 27–36, https://doi.org/10.5491/SHAW.2013.4.1.27
- 31 Steiger, A.E., Allemand, M., Robins, R.W. et al. (2014) Low and decreasing self-esteem during adolescence predict adult depression two decades later. *J. Pers. Soc. Psychol.* **106**, 325–338, https://doi.org/10.1037/a0035133
- 32 Fan, L.B., Blumenthal, J.A., Watkins, L.L. et al. (2015) Work and home stress: associations with anxiety and depression symptoms. *Occup. Med.* 65, 110–116, https://doi.org/10.1093/occmed/kqu181
- 33 Belanoff, J.K., Kalehzan, M., Sund, B. et al. (2001) Cortisol activity and cognitive changes in psychotic major depression. *Am. J. Psychiatry* **158**, 1612–1616, https://doi.org/10.1176/appi.ajp.158.10.1612
- 34 Stetler, C. and Miller, G.E. (2011) Depression and hypothalamic-pituitary-adrenal activation: a quantitative summary of four decades of research. *Psychosom. Med.* **73**, 114–126, https://doi.org/10.1097/PSY.0b013e31820ad12b
- 35 Grynderup, M.B., Kolstad, H.A., Mikkelsen, S. et al. (2013) A two-year follow-up study of salivary cortisol concentration and the risk of depression. *Psychoneuroendocrinology* **38**, 2042–2050, https://doi.org/10.1016/j.psyneuen.2013.03.013
- 36 Pruessner, J.C., Hellhammer, D.H. and Kirschbaum, C. (1999) Burnout, perceived stress, and cortisol responses to awakening. *Psychosom. Med.* **61**, 197–204, https://doi.org/10.1097/00006842-199903000-00012
- 37 Kirschbaum, C., Wolf, O.T., May, M. et al. (1996) Stress-and treatment-induced elevations of cortisol levels associated with impaired declarative memory in healthy adults. *Life Sci.* 58, 1475–1483, https://doi.org/10.1016/0024-3205(96)00118-X
- 38 Lupien, S.J., De Leon, M., De Santi, S. et al. (1998) Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nat. Neurosci.* **1**, 69–73, https://doi.org/10.1038/271

- 39 Pivonello, R., Isidori, A.M., De Martino, M.C. et al. (2016) Complications of Cushing's syndrome: state of the art. *Lancet Diabetes Endocrinol.* **4**, 611–629
- 40 Stokes, P.E. (1995) The potential role of excessive cortisol induced by HPA hyperfunction in the pathogenesis of depression. *Eur. Neuropsychopharmacol.* 5, 77–82, https://doi.org/10.1016/0924-977X(95)00039-R
- 41 Joseph, J.J. and Golden, S.H. (2017) Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus. *Ann. N. Y. Acad. Sci.* **1391**, 20–34, https://doi.org/10.1111/nyas.13217