



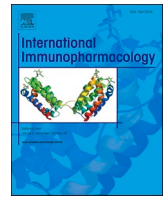
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The dynamic changes of cellular immunity among frontline medical workers who supported Wuhan for fighting against the COVID-19

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ABSTRACT

The outbreak of novel coronavirus disease 2019 (COVID-19) poses a great stress to frontline medical workers. Our previous study indicated that immune cells in the peripheral blood of frontline medical workers changed significantly. However, the dynamic changes of immune cells of frontline medical workers remain unclear. Here, we reported the dynamic changes of lymphocyte subsets in the peripheral blood of 51 frontline medical worker. The frontline medical workers struggling with COVID-19 from February 8 to March 31, 2020. Demographic and clinical data, including routine blood test data were extracted from the electronic health examination record and retrospectively analyzed. The lymphocyte (LYM) count and LYM ratio increased while the monocyte (MONO) ratio, neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR) and neutrophil (NEUT) ratio in the peripheral blood of frontline medical workers decreased 10 days after struggling with COVID-19. Interestingly, the differences of LYM count, LYM ratio, MONO ratio, NLR, NEUT ratio were more significantly in nurse than doctor. The differences of LYM ratio, NLR and NEUT ratio were more significantly in female than male. However, the changes of LYM count, LYM ratio, MONO ratio, NLR, MLR, NEUT ratio returned to the baseline 10 months after struggling with COVID-19. Together, these data indicated that immune cells in the peripheral blood changed significantly 10 days after struggling with COVID-19, but returned to normal after 10 months. Those maybe caused by psychological stress and we recommend to pay more attention to mental health and immune response of frontline medical workers.

1. Introduction

Novel coronavirus disease 2019 (COVID-19) was caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and outbreak as a pandemic because of the rapid global spread of the disease [1]. The mental health of frontline medical workers has been greatly challenged during the spread of the infectious disease [2,3]. Previous studies reported that severe acute respiratory syndrome (SARS) outbreak caused great psychological pressure on healthcare workers [4,5]. As expected, the critical situation of COVID-19 outbreak caused mental burden on healthcare workers [6–8]. A recent study revealed that healthcare workers in hospitals equipped with fever clinics or wards for patients with COVID-19 in China, experienced psychological burden,

especially nurses, women, those in Wuhan, and frontline healthcare workers directly engaged in the diagnosis, treatment, and care for patients with COVID-19 [9]. Similarly, Cai et al., reported frontline medical workers had more mental problems than non-frontline medical workers [10]. Such, more attention should be paid to mental health of frontline medical workers.

The immune cells in peripheral circulation are essential for against harmful pathogens. The number of white blood cell (WBC) and subset immune cells in the blood provides an important representation of the immune function. Immune system is regulated by neuroendocrine system [11]. Psychological stress regulates immune system also through neuroendocrine system, including the activation of the sympathetic nervous system (SNS) and hypothalamus–pituitary–adrenal

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cortex (HPA) axis, which release neurotransmitters [12,13]. Psychological stress has great impact on immune system [14], however, chronic stress usually suppresses the immune function [15]. Our previous study indicated that the immune cells in the peripheral blood of frontline medical workers who supported Wuhan for fighting against the COVID-19 changed when compared with controls [16]. The effects of COVID-19 outbreak on medical workers' mental health not only short-term but also long-term impacts according to the experience of medical workers responded to SARS [17]. But the dynamic changes of lymphocyte subsets in the peripheral blood of frontline medical workers remain unclear. Here, we reported the dynamic changes of lymphocyte subsets in the peripheral blood of 51 frontline medical workers from the Second Affiliated Hospital of Xi'an Jiaotong University who supported Wuhan for fighting against the COVID-19.

2. Material and methods

2.1. Participants

This retrospective study included frontline workers from the Second Affiliated Hospital of Xi'an Jiaotong University who supported Wuhan for fighting against the COVID-19 from February 8 to March 31, 2020 in Tongji Hospital of Huazhong University of Science and Technology. They went on vacation in a holiday resort in Baoji, Shaanxi, China from April 1 to May 5, and they started working normally after May 6. Those frontline medical workers were excluded if they have physical diseases and psychiatric diseases such as diabetes, hypertension, immune-mediated diseases, major depression, post-traumatic stress disorder, sleep disorder, anxiety and so on. Alcoholics and smokers were also excluded for the study. They underwent hematological test in January 2020, April 2020 and January 2021, respectively. A total 76 frontline medical workers meet the inclusion conditions but 25 frontline medical workers did not undergo hematological test in January 2021, 51 (67.1%) participated in the study. The COVID-19 virus nucleic acid were tested and the test results indicated them were negative for COVID-19 infection. The study was approved by the Ethics Committee of Xi'an Jiaotong University College of Medicine.

2.2. Data collection

Through the electronic health examination record system of our hospital, we collected the demographic and clinical data, including age, sex, occupation, fasting blood sugar (FBS), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) and medical history. Routine blood test before supporting Wuhan for fighting against the COVID-19 were tested in January 2020 and recorded as pre-stress data. Similarly, routine blood test 10 days post-stress and 10 months post-stress after supporting Wuhan for fighting against the COVID-19 were tested in April 2020 and January 2021 and recorded as 10 days post-stress data, 10 months post-stress data, respectively. As our previous reported, routine blood tests were performed using an automatic blood cell analyzer (XN9000; Sysmex, Japan). Routine blood tests data included WBC count, neutrophil (NEUT) count, NEUT ratio, lymphocyte (LYM) count, LYM ratio, monocyte (MONO) count, MONO ratio, eosinophil (EOS) count, EOS ratio, basophilic granulocyte (BASO) count, and BASO ratio were collected [16]. The NEUT to LYM ratio (NLR) was calculated by dividing the NEUT count by the LYM count. Similarly, the MONO to LYM ratio (MLR) was calculated by dividing the MONO count by the LYM count. Data were stratified by sex and occupation to compare differences of immune cells.

2.3. Statistical analysis

All analyses were performed using IBM SPSS Statistics for Windows (Version 19.0). Data were presented as mean \pm standard deviation (SD). Student's *t*-test was used to test the differences between frontline

medical workers with different sex or occupation. One-way analysis of variance (ANOVA) followed by Bonferroni's post hoc test was used to test for differences in immune cells among three groups. Participants were divided into different layers on the basis of sex and occupation. Statistical significance was considered as $P < 0.05$.

3. Results

3.1. Demographic and clinical characteristics

A total of 51 frontline medical workers from the Second Affiliated Hospital of Xi'an Jiaotong University were enrolled in this study. The demographic and clinical characteristics of frontline medical workers are presented in Table 1. Among 51 frontline medical workers, 41 (80.4 %) were female and 10 (19.6 %) were male. There were 38 (74.5 %) nurses and 13 (25.5 %) doctors among the frontline medical workers. Among 41 female frontline medical workers, 35 were nurses and 6 were doctors. The mean age, BMI, SBP, DBP and FBS of 76 frontline medical workers were 34.5 ± 6.3 years old, 22.7 ± 2.7 Kg/m², 117.4 ± 12.9 mmHg, 75.3 ± 9.7 mmHg and 4.9 ± 0.4 mmol/L, respectively (Table 1). The BMI of female was lower than that of male ($P = 0.041$, Table 1). There were no statistical differences between female and male in age ($P = 0.257$), SBP ($P = 0.400$), DBP ($P = 0.147$) and FBS ($P = 0.204$, Table 1). Nurses were younger than doctors ($P = 0.009$) and the SBP ($P = 0.025$), DBP ($P = 0.017$) and FBS ($P = 0.016$) of nurses were lower than doctors (Table 1). There was no difference in BMI ($P = 0.141$) between nurses and doctors (Table 1).

3.2. Dynamic changes of lymphocyte subsets in the peripheral blood of frontline medical workers

Dynamic changes of lymphocyte subsets in the peripheral blood of frontline medical workers are presented in Table 2. The LYM count and LYM ratio were significantly higher 10 days post-stress ($2.23 \pm 0.64 \times 10^9$ /L and 39.53 ± 8.43 %) when compared with the pre-stress ($1.71 \pm 0.47 \times 10^9$ /L and 32.32 ± 6.51 %, all $P < 0.01$, Table 2). Interestingly, stratification analysis based on sex showed that the LYM ratio was significantly higher only in female subgroup while stratification analysis based on occupation showed that the LYM ratio and LYM count were significantly higher only in nurse subgroup (Table 2). However, the changes of LYM count and LYM ratio returned to the baseline 10 months post-stress (Table 2).

The MONO ratio were significantly lower 10 days after supporting Wuhan for fighting against the COVID-19 (5.16 ± 1.09 %) when compared with the pre-stress (6.31 ± 1.16 %, $P < 0.01$, Table 2). Similarly, stratification analysis based on occupation showed that the MONO ratio was significantly lower only in nurse subgroup (Table 2). The MONO ratio returned to the baseline 10 months after supporting Wuhan for fighting against the COVID-19 (Table 2).

The BASO count and BASO ratio were significantly higher 10 months post-stress ($0.03 \pm 0.02 \times 10^9$ /L and 0.54 ± 0.28 %) when compared with the pre-stress ($0.02 \pm 0.02 \times 10^9$ /L and 0.32 ± 0.33 %, all $P < 0.01$, Table 2). Stratification analysis based on sex showed that the BASO ratio and BASO count were significantly higher only in doctor subgroup (Table 2).

The NEUT ratio was significantly lower 10 days post-stress (53.17 ± 8.68 %) when compared with pre-stress (59.47 ± 6.97 %; $P < 0.01$, Table 2). However, the change of NEUT ratio returned to the baseline 10 months after supporting Wuhan for fighting against the COVID-19 (Table 2). Stratification analysis based on sex and occupation showed that the NEUT ratio was significantly lower only in female subgroup and nurse subgroup (Table 2).

The NLR and MLR were significantly lower 10 days post-stress (1.47 ± 0.62 and 0.14 ± 0.04) when compared with the pre-stress (1.96 ± 0.66 and 0.20 ± 0.06) (all $P < 0.01$, Table 2). Stratification analysis based on sex and occupation showed that NLR was significantly lower

Table 1
Demographic and clinical characteristics of participants.

Variable	Participants (n = 51)	Male (n = 10)	Female (n = 41)	P	Doctor (n = 13)	Nurse (n = 38)	P
Age (years)	34.5 ± 6.3	36.5 ± 5.4	34.0 ± 6.5	0.257	38.3 ± 7.0	33.1 ± 6.6 [#]	0.009
BMI (kg/m ²)	22.7 ± 2.7	24.3 ± 2.3	22.4 ± 2.6*	0.041	23.7 ± 2.5	22.4 ± 2.7	0.141
SBP (mmHg)	117.4 ± 12.9	120.5 ± 9.7	116.6 ± 13.6	0.400	124.2 ± 14.6	115.0 ± 11.6 [#]	0.025
DBP (mmHg)	75.3 ± 9.7	79.3 ± 10.6	74.3 ± 9.3	0.147	80.8 ± 11.7	73.4 ± 8.3 [#]	0.017
FBS (mmol/L)	4.9 ± 0.4	5.1 ± 0.3	4.9 ± 0.4	0.204	5.2 ± 0.3	4.9 ± 0.4 [#]	0.016

M = male; F = female; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure, FBS = fasting blood sugar. *p < 0.05 vs male; [#]p < 0.05, ^{##}p < 0.01 vs doctor. Student's *t*-test was used to test the differences of continuous variables between two groups.

only in female subgroup and nurse subgroup (Table 2). Similarly, the changes of NLR and MLR returned to the baseline 10 months post-stress (Table 2). However, the WBC count, NEUT count, EOS count and EOS ratio of frontline medical workers did not change after supporting Wuhan for fighting against the COVID-19.

4. Discussion

This study was the first time to report the dynamic changes of immune subsets in the peripheral blood of frontline medical workers who fighting against the COVID-19. First, we found that the LYM count and LYM ratio increased while the MONO ratio, NLR, MLR and NEUT ratio in the peripheral blood of frontline medical workers decreased 10 days post-stress. Second, we found the changes of LYM count, LYM ratio, MONO ratio, NLR, NEUT ratio were based on sex and occupation. Finally, the changes of LYM count, LYM ratio, MONO ratio, NLR, MLR, NEUT ratio returned to the baseline 10 months after fighting against the COVID-19.

The outbreak of COVID-19 poses a great stress and challenge to frontline medical workers [10,18,19]. More and more medical workers have been infected with COVID-19 [20]. Zhou et al., recently reported that the prevalence of depressive symptoms, anxiety symptoms, somatization symptoms, insomnia and suicide risk in frontline medical staff were 57.6%, 45.4%, 12.0%, 32.0% and 13.0%, respectively while Lai et al., reported that depression, anxiety symptoms and insomnia accounted for 50.4%, 44.6%, and 34.0% of the total medical staff [9,21]. Ren et al., reported that 31.2% of the nurses in Wuhan, China were reported with a high-level depression and presented more severe psychological symptoms [22]. Similarly, anesthetist-intensivist in Italy reported high work-related stress (71.1%), insomnia (36.7%), anxiety (27.8%), and depression (51.1%) [23]. A prospective study reported occupational stress of health care workers was significantly associated with anxiety and depression. The doctors reported high levels of distress (73%), sleep problems (28%), anxiety (25%), and depression (64%) [24]. These results indicated frontline medical workers suffered from psychological stress. Psychological stress has great impact on immune system through activating nervous system [25–27]. Previous studies indicated that psychological stress regulates the redistribution of leukocytes through stress responses by activating the SNS and HPA axis, which release catecholaminergic neurotransmitters and corticosterone [12,13,28,29]. In this study, we found that the LYM count and LYM ratio increased while the MONO ratio, NLR, MLR and NEUT ratio in the peripheral blood of frontline medical workers decreased 10 days post-stress. The changes of immune cells of the frontline medical workers may be caused by psychological stress. Moreover, the changes of immune cells in the peripheral blood of frontline medical workers may make them more susceptible to COVID-19. We think mental health and immune status of frontline medical staff should be paid more attentions.

In this study we also found the changes of LYM ratio, NLR and NEUT ratio were more significantly in female than male. Interestingly, Lai et al., reported that female frontline medical staff experienced more

psychological burden than male frontline medical staff [9]. Similarly, Zhou et al., reported that female gender was positively associated with anxiety symptoms in frontline medical staff, which was very similar to our results [21]. This finding may be because females are more sensitive to stress than males. Numerous studies conducted that the stress response depend on sex, which caused by adrenal and gonadal [30,31]. Testosterone, from male, is negatively correlated with the activation of HPA axis while estrogen, from female, is positively correlated with the activation HPA axis [32,33]. Previous study indicated that females were more likely to experience stress and develop anxiety [6]. Female responded to acute stressors in a more pro-inflammatory fashion with increased mobilization of immune cells than male [34]. On the other hand, nurses treating patients with COVID-19 are likely exposed to the highest risk of infection because of their close, frequent contact with patients and working longer hours than usual [9]. In our study, 85% of female frontline medical workers were nurses, so high infection risk and heavy workload may be another reason of the finding.

In this study, there were 38 (74.5%) nurses and 13 (25.5%) doctors. Another interesting finding of our study was that changes of LYM count, LYM ratio, MONO ratio, NLR, NEUT ratio were more significantly in nurse than doctor. We think the main reason for this was that 35 of 38 nurses were female and the immune response of female frontline medical staff was more significant than male. Second, recently study report that daily working hours are a risk factor for psychological disturbances of frontline medical staff [21]. Nurses maintained close and frequent contact with COVID-19 patients, and worked longer than usual. Finally, Kang et al., reported that the mental health burden of frontline medical workers particularly heavily on young women [2]. Zhou et al., reported that age was negatively associated with the symptoms of depression, anxiety and insomnia of frontline medical workers [21]. In our study, nurses were younger than doctors, with limited experiences regarding the infectious pandemic; thus, inevitably leading to psychological problems. Third, as mentioned above, the higher infection risk and heavier workload among nurses may be another reason of the finding.

Our government has set up multidisciplinary mental health teams to reduce the negative psychological impact of COVID-19 on medical workers [35]. Our hospitals also provided essential services such as 1 month of vacation in a holiday resort, daily living supplies for their families and so on, to reduce the negative psychological impact of COVID-19 on medical workers. The frontline medical workers were also honored as heroes by people. We also investigated the changes of immune subsets in the peripheral blood of frontline medical workers 10 months after struggling with COVID-19 because our hospital provides health examination for some employees in January every year. As expected, the changes of LYM count, LYM ratio, MONO ratio, NLR, MLR, NEUT ratio in the peripheral blood of frontline medical workers returned to the baseline 10 months after fighting against the COVID-19.

This study has several limitations. First, our study is a small sample, single-center retrospective study, because the clinical data of most frontline medical workers before the COVID-19 outbreak was not available. Only 76 frontline medical workers meet the inclusion

Table 2
Comparison of immune factors in controls and stress group.

Variable	Pre-stress	10 Days Post-stress	10 Months Post-stress	P	
WBC (10 ⁹ /L)	5.37 ± 1.20	5.73 ± 1.34	5.41 ± 1.42	0.318	
	Male	5.79 ± 1.56	6.38 ± 1.34	5.55 ± 1.20	0.397
		Female	5.26 ± 1.10	5.57 ± 1.31	5.38 ± 1.47
	Doctor		5.42 ± 1.24	6.34 ± 1.40	5.49 ± 1.40
	Nurse	5.35 ± 1.20	5.52 ± 1.27	5.39 ± 1.44	0.828
	NEUT (10 ⁹ /L)	3.22 ± 0.94	3.09 ± 0.99	3.15 ± 1.10	0.797
Male		3.36 ± 1.10	3.26 ± 0.87	3.17 ± 0.88	0.899
		Female	3.19 ± 0.91	3.04 ± 1.02	3.14 ± 1.16
Doctor			3.10 ± 0.64	3.29 ± 0.74	3.00 ± 0.85
Nurse		3.26 ± 1.02	3.01 ± 1.06	3.20 ± 1.18	0.592
LYM (10 ⁹ /L)		1.71 ± 0.47	2.23 ± 0.64**	1.77 ± 0.53##	<0.001
	Male	1.93 ± 0.70	2.64 ± 0.76*	1.90 ± 0.65#	0.044
		Female	1.66 ± 0.39	2.14 ± 0.57**	1.74 ± 0.50##
	Doctor		1.84 ± 0.74	2.54 ± 0.82	1.98 ± 0.72
	Nurse	1.67 ± 0.34	2.13 ± 0.54**	1.70 ± 0.44##	<0.001
	MONO (10 ⁹ /L)	0.33 ± 0.07	0.29 ± 0.08	0.37 ± 0.11##	<0.001
Male		0.38 ± 0.07	0.33 ± 0.07	0.36 ± 0.08	0.40
		Female	0.32 ± 0.07	0.28 ± 0.08	0.37 ± 0.11##
Doctor			0.36 ± 0.08	0.35 ± 0.07	0.38 ± 0.10
Nurse		0.33 ± 0.08	0.27 ± 0.07*	0.36 ± 0.11##	<0.001
EOS (10 ⁹ /L)		0.08 ± 0.06	0.10 ± 0.05	0.09 ± 0.07	0.494
	Male	0.11 ± 0.09	0.12 ± 0.05	0.10 ± 0.05	0.709
		Female	0.08 ± 0.05	0.09 ± 0.05	0.09 ± 0.07
	Doctor		0.10 ± 0.08	0.13 ± 0.05	0.11 ± 0.05
	Nurse	0.08 ± 0.06	0.09 ± 0.05	0.09 ± 0.07	0.574
	BASO (10 ⁹ /L)	0.02 ± 0.02	0.02 ± 0.01	0.03 ± 0.02**	0.004
Male		0.01 ± 0.02	0.03 ± 0.02*	0.03 ± 0.02*	0.039
		Female	0.02 ± 0.02	0.02 ± 0.01	0.03 ± 0.02*
Doctor			0.01 ± 0.02	0.03 ± 0.02	0.03 ± 0.02*
Nurse		0.02 ± 0.02	0.02 ± 0.01	0.03 ± 0.02	0.067
NLR		1.96 ± 0.66	1.47 ± 0.62**	1.88 ± 0.75##	0.001
	Male	1.83 ± 0.57	1.30 ± 0.42	1.80 ± 0.75	0.072
		Female	2.00 ± 0.68	1.51 ± 0.66**	1.90 ± 0.78#
	Doctor		1.85 ± 0.58	1.36 ± 0.34	1.63 ± 0.56
	Nurse	2.00 ± 0.68	1.51 ± 0.69**	1.94 ± 0.79#	0.005
	MLR	0.20 ± 0.06	0.14 ± 0.04**	0.22 ± 0.06##	0.001
Male			0.13 ± 0.04*	0.20 ± 0.07#	0.015

Table 2 (continued)

Variable	Pre-stress	10 Days Post-stress	10 Months Post-stress	P	
WBC (10 ⁹ /L)	0.21 ± 0.07				
	Female	0.20 ± 0.06	0.14 ± 0.04**	0.22 ± 0.06##	<0.001
		Doctor	0.21 ± 0.06	0.15 ± 0.04**	0.21 ± 0.07#
	Nurse		0.20 ± 0.07	0.13 ± 0.04**	0.22 ± 0.06##
		NEUT ratio (%)	59.47 ± 6.97	53.17 ± 8.68**	57.29 ± 8.90#
	Male		57.84 ± 6.63	50.87 ± 7.37	56.86 ± 7.66
Female			59.87 ± 7.07	53.73 ± 8.96**	57.40 ± 9.26
	Doctor		57.90 ± 6.78	52.18 ± 5.01	54.66 ± 6.24
Nurse	60.01 ± 7.03		53.51 ± 9.65**	58.19 ± 9.55	0.005
LYM ratio (%)	32.32 ± 6.51		39.53 ± 8.43**	33.50 ± 8.04##	<0.001
	Male	33.37 ± 6.83	41.47 ± 8.00	34.31 ± 8.34	0.054
		Female	32.06 ± 6.49	39.05 ± 8.56**	33.30 ± 8.06##
	Doctor		33.24 ± 6.80	39.72 ± 5.96	35.84 ± 7.53
	Nurse	32.01 ± 6.47	39.46 ± 9.19**	32.70 ± 8.14##	<0.001
	MONO ratio (%)	6.31 ± 1.16	5.16 ± 1.09**	6.88 ± 1.42##	<0.001
Male		6.74 ± 1.42	5.26 ± 0.91*	6.48 ± 1.20#	0.022
		Female	6.20 ± 1.08	5.14 ± 1.14**	6.97 ± 1.46##*
Doctor			6.77 ± 1.41	5.61 ± 1.09	6.89 ± 1.15#
Nurse		6.15 ± 1.04	5.01 ± 1.06**	6.87 ± 1.51##*	<0.001
EOS ratio (%)		1.58 ± 1.18	1.70 ± 1.08	1.80 ± 1.38	0.682
	Male	1.86 ± 1.31	1.96 ± 0.81	1.82 ± 1.03	0.956
		Female	1.51 ± 1.16	1.64 ± 0.89	1.79 ± 1.47
	Doctor		1.86 ± 1.16	2.03 ± 0.76	1.98 ± 1.01
	Nurse	1.48 ± 1.19	1.59 ± 0.90	1.74 ± 1.49	0.658
	BASO ratio (%)	0.32 ± 0.33	0.44 ± 0.27	0.54 ± 0.28**	0.002
Male		0.19 ± 0.30	0.44 ± 0.25	0.53 ± 0.29*	0.028
		Female	0.36 ± 0.34	0.44 ± 0.28	0.54 ± 0.28*
Doctor			0.24 ± 0.34	0.47 ± 0.36	0.62 ± 0.33*
Nurse		0.35 ± 0.33	0.43 ± 0.24	0.51 ± 0.26	0.055

Pre-stress = blood test data of medical workers before providing medical service for COVID-19 patients; WBC = white blood cell; NEUT = neutrophil; LYM = lymphocyte; MONO = monocyte; EOS = eosinophil; BASO = basophilic granulocyte; NEUT = neutrophil; NLR = neutrophil-to-lymphocyte ratio; MLR = monocyte-to-lymphocyte ratio. *p < 0.05, **p < 0.01 vs pre-stress; #p < 0.05, ##p < 0.01 vs 10 days post-stress. Continuous variables were analyzed using one-way ANOVA test.

conditions and the clinical data before the COVID-19 outbreak was available, but 25 frontline medical workers did not undergo hematological test in January 2021, so only 51 participated in the study. Our study revealed a phenomena, psychological stress can temporarily affect immune cells but the conclusion need to be verified by high-quality clinical studies. Second, although frontline medical workers with physical diseases and psychiatric diseases such as diabetes,

hypertension, immune-mediated diseases, major depression, post-traumatic stress disorder, sleep disorder, anxiety, smoking and drinking were excluded for the study. Regular physical activity and healthy sleeping habits help preventing hematopoietic changes. Unfortunately, frontline workers experienced excessive workload and reduced physical activity. Our study did not address other potential confounding factors, such as diet, lifestyle choice, and life events. Third, our study only investigated the changes of immune cells in the peripheral blood, the changes of the level of cytokines and the function of immune cells also need to be measured in future. And the correlation between the changes immune cells and mental status such as depression, anxiety, stress, and post-traumatic stress disorder, should also be studied. Finally, the levels of stress hormones, such as glucocorticoid, adrenaline and noradrenaline, of frontline doctors and nurses should also be detected.

5. Conclusion

In summary, our data indicated that immune cells in the peripheral blood of frontline medical workers changed significantly 10 days after supporting Wuhan for fighting against the COVID-19, especially in females and nurses, but returned to normal after 10 months. Those maybe caused by psychological stress and we recommend to pay more attention to mental health and immune status of frontline medical workers.

Author Contributions

Participated in research design: Wei Jiang, Juanjuan Yang and Zongfang Li. Collected the clinical data: Juanjuan Yang, Qian Wang, Shuqun Zhang and Wei Jiang. Analyzed the clinical data: Juanjuan Yang, Wei Jiang and Qian Wang. Wrote and contributed to the writing of the manuscript: Juanjuan Yang, Wei Jiang and Zongfang Li.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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