How to Cite:
Soetrisno, S., Nurinasari, H., Cahyanto, E. B., Maulina, R., Nurhidayati, S., Arifa, H. N. A., Jayanti, C. D., Ansori, A. N. M., Rahmawati, N. Y., & Novika, R. G. H. (2022). The effect of psycho-curative towards anxiety, cortisol, and PIBF level of pregnant woman during COVID-19 pandemic. *International Journal of Health Sciences*, *6*(S2), 528–540. https://doi.org/10.53730/ijhs.v6nS2.5017

The Effect of Psycho-Curative Towards Anxiety, Cortisol, and PIBF Level of Pregnant Woman During COVID-19 Pandemic

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International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 27 Nov 2021, Manuscript revised: 09 Feb 2022, Accepted for publication: 18 March 2022

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***Abstract*---**Managing stress plays a vital role in building a healthier support system for pregnancy and increased fetal growth. However, many pregnant women undergo stress during the COVID-19 pandemic. Cortisol is associated with early miscarriage derived by the adrenal glands responding to stress. In addition, anxiety has side effects on women's quality of life. PIBF mediates the immunomodulatory effects of progesterone during pregnancy. This study aimed to measure the changes in anxiety, cortisol, and PIBF, levels in the pregnant woman due to increased stress during the COVID-19 pandemic. This study was conducted in Community Health Center Surakarta, Indonesia. This study used twenty pregnant women and classified into two groups. The control group was given regular prenatal assessment, while the treatment group was given a psychocurrative intervention, including cognitive, social, spiritual, and physical support. This intervention was performed once a week in a class and twice at their homes. Blood was collected from the pregnant woman to measure PIBF and cortisol levels before and after the intervention. In addition, anxiety was measured using the DASS-21 scale.

***Keywords*---**anxiety, cortisol, PIBF, pregnant women, psychocurative.

Introduction

Coronavirus (COVID-19) is caused by SARS-CoV-2 in human. This condition triggers risk of women in mental health conditions, particularly perinatal anxiety and stress (Novika *et al.*, 2019). A long-term study of pandemic affects pregnant and non-pregnant mothers. Pregnant women have higher depression and anxiety scores than non-pregnant women (Hamzehgardeshi *et al.*, 2021; Villar *et al.*, 2021). These conditions trigger more anxiety and stress in pregnant women (Novika *et al.*, 2019; van den Heuvel *et al.*, 2015). Antenatal depression is often undiagnosed and untreated, whereas the available treatment for psychological problems, including anti-depressants and breastfeeding risks. In addition, barriers to therapy such as stigma and expenses are prohibited for women. Therefore, regular assessment of women's mental health is urgently needed. Generally, women need consultation about their mental health during the visit. For this reason, health facilities must provide more services to women who are pregnant in pandemic situation (López-Morales *et al.*, 2021). Approximately, 2% of pregnant women experienced with anxiety severe, 32% moderate-severe, 42%

moderate, 23% mild, and only 2% did not experience anxiety due to the pandemic (Viandika and Septiasari, 2021).

The psychological intervention impact on prenanat women in pandemic situation according to meta-analysis and systematic reviews studies. There were 42% of anxiety prevalence and 25%. Several factors, such as age, family condition, physical activity, and social support influence mental health of pregnant women in COVID-19 pandemic condition. For this reason, an effort is needed to prevent mental health disorders (Fan *et al.*, 2021). Pregnant women need better cognitive support during pregnancy (Khoury *et al.*, 2021). In terms of mental disorders, pregnant women also experience physical complaints such as fever, cough, pneumonia, and other immunological disorders (Abedzadeh-Kalahroudi *et al.*, 2021).

A study reported that lymphocytes express progesterone-induced blocking factors (PIBF) in pregnancy. PIBF is critical to regulate immunological actions to protect and maintain a pregnancy (Szekeres-Bartho, 2018). However, fetal exposure to excessive maternal cortisol could impact human pregnancy loss and dysfunctional brain development to infancy and childhood (Nepomnaschy *et al.*, 2006; Scheinost *et al.*, 2017). In early pregnancy, maternal cortisol slower the development rate of infant according to Bayles Scales of Infant Development (BSID), behavioral and emotional disturbance during infancy and childhood (Bergman *et al.*, 2007; Davis and Sandman, 2010). These two factors are prominent in maternal and fetal well-being (Rauf *et al.*, 2021).

Psychocurative is a psychological intervention that ensures a person against their mental state, including cognitive, social, physical, and spiritual (Soetrisno *et al.*, 2020). This intervention can be adjusted to psychological conditions and build a harmonious relationship to improve psychological stability (Soetrisno *et al.*, 2019). Long-term (two years) psychocurrative reduces anxiety, cortisol, and depression levels. Furthermore, a study reported that psychocurrative improves the condition in advanced cervical cancer patients (Soetrisno *et al.*, 2020). Therefore, this study aimed to analyze the level of anxiety, cortisol, and PIBF towards pregnant women due to increased stress in COVID-19 pandemic situation.

Method

Participant

Based on the screening questionnaire, the first trimester of pregnant women who experienced stress was selected from Sibella Community Health Center Surakarta, Indonesia. Pregnant women with severe cardiovascular or other physical diseases who refused to participate were excluded. All participants were received written and informed consent. This study was approved by the Research Ethics Committee of Faculty of Medicine, Universitas Sebelas Maret, Indonesia (Number 35/UN27.06.6.1/EC/2021).

Study design

This study was a quasi experimental using the pretest-posttest control group design. The anxiety level between two groups of pregnant women before intervention was measured by the depression anxiety stress scale-21 (DASS-21). Then, psychocurrative intervention was conducted in the intervention group. This study was performed at Community Health Center in Surakarta, Indonesia. A trained midwife guided psychocurrative to intervention about cognitive, social, spiritual, and physical support. Cognitive support was an approach to provide information to pregnant women about COVID-19 definitions, clinical symptoms, laboratory tests, transmission, prevention, and activities of pregnant women during a pandemic. The husband, the family, instrumental/material, and emotional support from husband. Spiritual support provided positive support in accordance with the religion embraced, including truth, goodness, and justice. Physical support was given training to a pregnant woman on muscle relaxation. This intervention was performed once a week in a class and twice at their homes. The respondents were given a psychocurrative book. A relaxation class using the audiovisual method were scheduled for one hour from 9-10 A.M. in Community Health Center, Surakarta, Indonesia, with strict regulation of COVID-19 protocols. The control group was given a regular prenatal assessment in Community Health Center, such as examining haemoglobin, sexual transmitted disease (STD) infection, hepatitis B, urine, and glucose. They were given counselling based on their examination and anamnesis.

Instruments

The depression anxiety stress scale-21 (DASS-21) which developed by Lovibond was used to measure anxiety in pregnant women. The DASS 21 instruments consisted of 21 question items, including physical, emotional/psychological and behavioural variables. Stress level on the DASS 21 was classified into five levels, including normal, mild, moderate, severe, and very severe ranges were 0-7; 8-9, 10-12, 13-16, and 17, respectively (Henry and Crawford, 2005). The scale rate was classified into 3 categories, namely: 0 = Not agree; 1= Appropriate to some degree or rarely; 2= Appropriate to frequent extent; and 3 = strongly agree.

Measurement of cortisol and PIBF level

Cortisol and PIBF levels of serum were measured by ELISA (Multi-Science, China) based on the manufacturer's instructions. The coefficient variations of intra- and inter-assay were as follows: cortisol (7.43-8.78%; <7.03-8.96%), and PIBF (4.93-5.50%; <3.86-7.27%). Tetramethylbenzidine substrate (Sigma-Aldrich) was used to develop plates, then stopped using 2 N H2SO4, and read at a dual-wavelength of 450 nm in a microplate reader (BIO-RAD, USA) to gain the concentration and optical density (OD) values.

Statistical analysis

The data were analysed by SPSS version 22.0 for windows. Data were presented as mean±SD, frequency and percentage (%). All study variables were analysed by

an independent t-test. P-value ≤0.05 was considered as a significant difference statistically.

Results and Discussion

The respondent's characteristics are presented in Table 1. The intervention group's mean maternal and gestational ages were 29.4 years and 14.6 weeks. The primigravida and multigravida were 1 (10%) and 9 (90%), respectively. The respondents in the intervention group were 2 (20%) people who did not have a child, 4 (40%) people with a child, and 4 (40%) people with more than four children. The control group's maternal ages and gestational week were 23 years old and 16.6 weeks. The primigravidas were 8 (80%) and 2 (20%). The women's demographic data are presented in Table 1 (n=20).

Table 1
Demographic characteristic of respondents

Characteristics		Intervention group	Control group
Maternal ages (year)	M±SD	29.4±2.86	23±4.4
Gestational age (week)	M±SD	14.6±4.52	16.6±3.97
Gravida			
1 (Primigravida)	N (%)	1 (10%)	8 (80%)
>1 (Multigravida)	N (%)	9 (90%)	2 (20%)
Parity (no. of live births) (%)			
0	N (%)	2 (20%)	8 (80%)
1	N (%)	4 (40%)	1 (10%)
>1	N (%)	4 (40%)	1 (10%)
History of abortion (%)	N (%)	0 (0%)	1 (100%)

We further examined the effect of pandemic COVID-19 against the anxiety level in pregnant women. As shown in Figure 1, a higher level of anxiety was found in pregnant woman before the intervention in both groups, however we did not detect significant differences of anxiety level before and after psychocurrative intervention in both groups according to the paired sample t-test (p=0.591 and p=0.162).

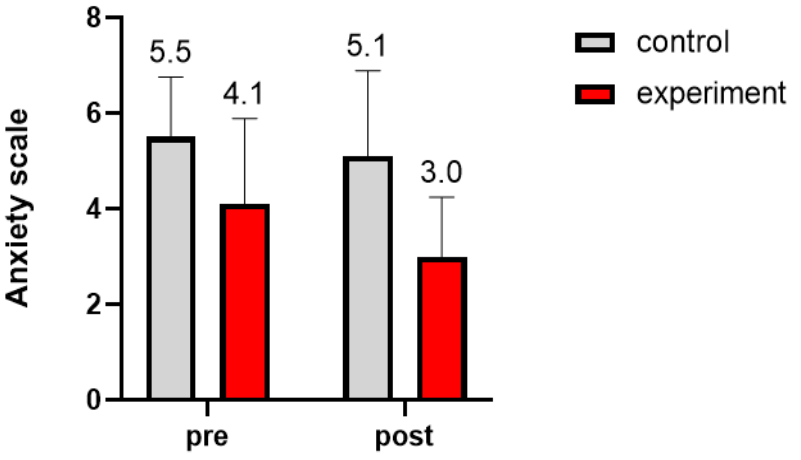

Figure 1. The differences of mean anxiety level between group pre and post intervention

*Significant vs before intervention in the same group, p<0.05. Control group was given regular prenatal assessment, while experiment group was given psycho-curative intervention

Next, we evaluated the level of cortisol in pregnant women between the control group and the experimental. Our study showed that the highest average level of cortisol in pregnant woman was occurred in control group after the psychocurrative intervention. We observed a significant difference between pre-post-test intervention in both group (p= 0.05 and p= 0.000) based on paired sample t-test (Figure 2).

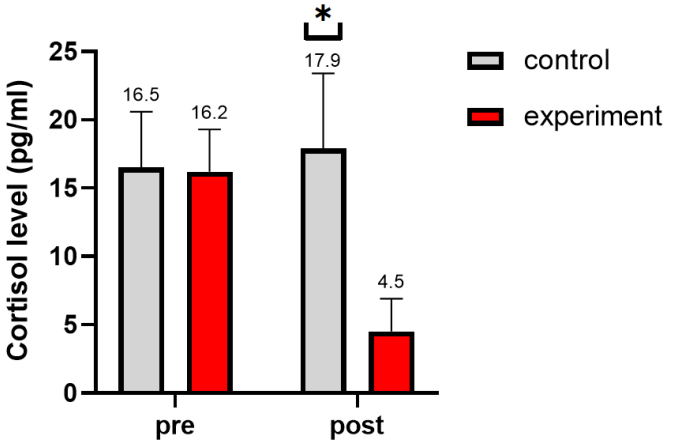

Figure 2. The differences of mean Cortisol level between group pre and post intervention

*Significant vs before intervention in the same group, p<0.05. Control group was given regular prenatal assessment, while experiment group was given psycho-curative intervention

As shown in Figure 3, the average PIBF level increased in both group after the intervention. We detected a significant difference of PIBF level before and after the psychocurrative intervention in the experiment group (p=0.023). Unfortunately, no significant difference was found in the control group (p= 0.610) according to the paired sample t-test.

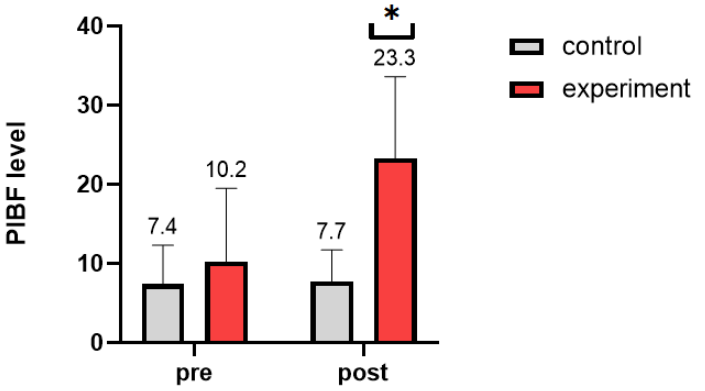

Figure 3. The differences of mean PIBF level between group pre and post intervention

*Significant vs before intervention in the same group, p<0.05. Control group was given regular prenatal assessment, while experiment group was given psycho-curative intervention

Anxiety and cortisol had adverse effect to pregnancy. The anxiety and cortisol levels were higher in the control group (Mean=5.1, Mean=17.9) comparing to the experiment group (Mean=3, Mean=4.58). However, PIBF level were higher in the experimental group (Mean=23.37). Our result study showed a higher of the anxiety and cortisol levels in the control group than the experiment group (P<0.05). We also observed a higher PIBF level in experimental group than the control group according to the independent t-test (Table 2).

Table 2
The difference of anxiety scale, cortisol level, and PIBF level between the control and experimental group after the intervention (n=20)

	Control Group			Experimental Group			t	p-value
	n	Mean	SD	n	Mean	SD		
Anxiety scale	10	5.1	1.79	10	3.0	1.24	3.042	<0.05
Cortisol level	10	17.9	5.59	10	4.58	2.49	6.898	<0.00
PIBF level	10	7.7	4.06	10	23.37	10.34	4.455	<0.00

This randomized controlled trial (RCT) study proved that psycocurrative could reduce DASS-21 score in pregnant women's control and treatment groups.

Anxiety in pregnant women is influenced by several factors, including psychological and physiological changes. Pregnant women have high risk of anxiety due to COVID-19 pandemic (Hamzehgardeshi *et al.*, 2021; Villar *et al.*, 2021). Additionally, several psychiatric problems such as anxiety and depression are related to pregnant women during COVID-19 pandemic (Salari *et al.*, 2020). A previous study showed that the COVID-19 pandemic elevates anxiety and depression in pregnant women Durankuş and Aksu, 2022). COVID-19 in Indonesia, causes the highest death of pregnant women globally. A previous study from the cohort data showed that several pregnant women from different ethnic groups experienced worse mental health due to financial problems (Prady *et al.*, 2013). Psycocurrative, involving cognitive counseling, social, spiritual, and physical support for pregnant women, revealed to build an excellent concept of women's pregnancy. Psycocurrative helps pregnant women alleviate the stress by recognizing the spiritual aspect to find meaningful life (Ito *et al.*, 2014). The abundance of cognitive and spiritual value will change the perception of their life and pregnancy (Koenig, 2012). By this mechanism, the pregnant woman changes their distress to a eustress condition or tends to lower the stress feelings by having psychocurative aids. Psychocurrative changes distress into eustress in 15 advanced-stage cervical cancer patients after intervention ($p<0.001$) (Soetrisno *et al.*, 2019). Mind-body exercises, which emphasize mindfulness during physical and psychological support, can help the body to lighten the stress.

In this study, cortisol and PIBF levels were measured to understand the therapeutic mechanism of Psycocurative in pregnant women. Cortisol level was measured because the excessive level of cortisol during pregnancy was related to stress. Moreover, preterm birth and low birth weight increases during COVID-19 pandemic (Cook et al., 2018; Mah et al., 2019). On the other hand, PIBF can maintain a healthy pregnancy and a prognostic biomarker to threaten miscarriage (Lim *et al.*, 2020). In this study, psychocurative acts as an intervention that triggers a functional alteration of the brain through verbal and non-verbal interactions between therapist and respondents, empathy, catharsis, cognitive restructuring and new learning. Positive and mutual interaction between therapist and respondents would have mutual neuronal machinery, which stimulates neural plasticity and neurogenesis. Psychocurative provides a suitable environment to develop cognitive, spiritual, and social abilities. The therapist and the respondents can perform controlled exposure against stress due to a supportive environment during psychocurative. It benefits to handle the stress in the future (Malhotra and Sahoo, 2017). Traumatic experiences were submerged into unconscious memory that controls anxiety and fear from consciousness. Therefore, psychocurrative attempts to activate the respondents' emotions such as anxiety and fear to be released in a free controlled environment and leading to modification of maladaptive reactions. Thus, pregnant women level of anxiety is reduced. Another study demonstrated that psychological interventions decrease the level of depression and stress in pregnant and postpartum women. Psychological intervention is the effective approach to improve mental health in pregnant women and the puerperium to reduce stress and depression (Novika *et al.*, 2019).

Maternal anxiety was correlated with higher cortisol levels. A previous study found that higher prenatal anxiety predicted increases in cortisol levels (Kane *et*

al., 2014). Anxiety during pregnancy can be caused by socio-demographic status, adverse pregnancy outcomes, fear of COVID-19 infection, social restriction, and fear of not having a proper pregnancy treatment (Ali *et a*l., 2012; Lebel *et al.*, 2020). In a person under stress or anxiety, the hypothalamus gland releases corticotropin-releasing hormone (CRH) and stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH). Besides, the adrenal glands express cortisol. This mechanism is known as hypothalamus pituitary adrenal (HPA) axis (Kuepfer, 2010). This repeated process leads to an increase in cortisol levels which have adverse clinical effects, including the incidence of a social anxiety disorder (SAD) in children (Poole *et al.*, 2018). In addition, ACTH stimulates the synthesis of glucocorticoids in the adrenal cortex. Although figure 1 shows no significant difference in anxiety level between the control and experimental groups. Therefore, several efforts are needed to reduce anxiety during pregnancy, such as social support from family or health care professionals.

On the one hand, PIBF is a mediator produced by lymphocytes of pregnant women who have been sensitized by progesterone. Serum and urine can be detected PIBF in pregnant women (Shah *et al.*, 2018). PIBF is an attribute to a normal pregnancy that maintain successful pregnancy (Szekeres-Bartho and Polgar, 2010). In a study with pregnant mice, acoustic stress correlated with lower progesterone and PIBF in plasma, meaning that prenatal stress inhibits the production of PIBF. Therefore, in a healthy pregnancy, the PIBF level is higher than those who experience miscarriage (Szekeres-Bartho, 2018).

Psycocurative intrevation maintenaces haemostatic condition to the environment through a hormonal pathway involving the hypothalamus, pituitary glands and the adrenal cortex (Henry and Crawford, 2005; Szekeres-Bartho *et al.*, 2018). Stress condition triggers the change of eustress in the hypothalamus gland. This condition decreases corticotropin-releasing hormone (CRH) level, inhibit the pituitary gland to release adrenocorticotropic hormone (ACTH), and block the adrenal glands to release cortisol. These conditions decrease cortisol levels which have adverse clinical effects, including the incidence of social anxiety (Szekeres-Bartho and Polgar, 2010). Provision of non-relaxation techniques pharmacological alters cortisol and serotonin levels through the HPA axis mechanism to suppress cortisol hormone levels and increase levels of functioning serotonin as a mood stabilizer (Soetrisno *et al.*, 2019; Soetrisno *et al.*, 2020).

The human mind, brain, and immune system contribute to response toward external stimuli (Poole *et al.*, 2018). A previous study revealed the relationship between stress and health outcomes, including mortality and morbidity of the pregnant woman (Turner *et al.*, 2020). The ACTH accumulation increases risk factor of chronic diseases, pro-inflammatory immune dysregulation, and miscarriage (Poole *et al.*, 2018). The immune system is the most important system that prevents the fetus's damage. During pregnancy, the mother and fetus's immune systems influence each other. The mother's immune symaintainsntain the welfare of the mother and fetus. Additionally, the fetus impact on the mother's immune system against the environment.

The cortisol hormone can be reduced by psycocurative during psychological distress. The modulation of immune function is directly regulated through

immune cells and sympathetic nervous system. Another study demonstrated that stress factors inhibit T-helper 1 (Th1) activity; however, T-helper 2 (Th2) is overstimulated (Connor *et al.*, 2020). Additionally, previous studies have shown a shift favoring Th2 cytokine imbalance in response to stress. Based on the alloimmune theory, a successful pregnancy requires blocking factors to inhibit the maternal immune system's rejection of paternal antigens. Various studies have shown that progesterone plays a role in creating an adequate immune environment during early pregnancy, such as improving the chance of embryo implantation and reducing the risk of miscarriage (Awick *et al.*, 2017; Shah *et al.*, 2018). The psycocurative intervention can reduce social stressors and sympathetic activation. These conditions lead to reduce pro-inflammatory immune response. Therefore, psychocurrative intervention can affect the immune system (Soetrisno *et al.*, 2019; Soetrisno *et al.*, 2020).

This study provides insight into pregnant women who have anxious to have a better pregnancy experience. Psycocurative was recommended as an intervention during pandemic COVID-19. For pregnant women. Our finding study revealed that alteration of anxiety, cortisol, and PIBF levels after psycocurative intervention. Psychological intervention is an effective approach to reduce psychological stress during pregnancy. The previous studies also demonstrated the efficacy of psychological interventions to decrease depression and stress in pregnant and postpartum women. Therefore, implementing psychocurative can help pregnant women who suffer from stress and anxiety in primary health care.

Conclusion

In summary, anxiety, depression, and stress reduced in pregnant women after psychological intervention in the COVID-19 pandemic. Psychocurative reduced anxiety, cortisol, and increased PIBF levels in pregnant women, suggesting that psychological intervention could preserve the mental state during the COVID-19 pandemic. Therefore, it was needed to prevent an adverse outcome of pregnancy. Several efforts are required for further studies, such as the midwife needs to understand the psychological intervention to provide health quality care that consists of physical and mental intervention.

Acknowledgments

This work was supported by Universitas Sebelas Maret, Surakarta, Indonesia. Author sincerely thanks to the respondents and Sibela Community Health Center, Surakarta, Indonesia who kindly helped during the experiment.

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