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Interactive pregnancy education on stress, cortisol, and epinephrine level in primigravida of trimester III pregnant: a quasi-experimental

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Abstract
Infant mortality is caused by various health problems, especially since the gestation period, even starting before the gestation period. Stress during pregnancy affects the motor, cognitive, and emotional development of the baby. This study aims to determine the effect of interactive pregnancy education (IPE) on decreasing levels of cortisol, epinephrine, and its relationship with stress levels in third-trimester primigravida pregnant women. This research is a quasi-experimental study using a nonequivalent control group design, which has two groups, namely the experimental group and the control group. The authors compared the experimental group that was given the intervention with the control group that was not given any treatment. This research was conducted in the three Community Health Centers in Indonesia from June 2022 until December 2022. The samples were 30 third-trimester primigravida pregnant women for the intervention and control groups. Data were analyzed using the Mann–Whitney and Wilcoxon tests with SPSS 22 software. The results of this study indicate that IPE has a good impact on pregnant women, where there is a significant relationship in the post-test cortisol and epinephrine levels in the intervention group. This indicates that IPE contributed to the difference in post-test scores in the intervention group. The IPE method is effective in reducing stress levels and cortisol levels in pregnant women, especially in pregnant women with high levels of stress.

Keywords: cortisol levels, epinephrine levels, interactive pregnancy education (IPE) intervention, pregnant, stress, third-trimester primigravida

Introduction

The infant mortality rate is an indicator in determining the health level of a country. WHO reports that 4.1 million or 75% of all under-five deaths occur in the first year of life, whereas 47% of deaths occur during the neonatal period[1]. Infant mortality, especially in the early period of life, causes invaluable physical, psychological, and material losses[2]. Infant mortality is caused by various health problems, especially since the gestation period, even starting before the gestation period[3]. This is triggered by

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HIGHLIGHTS

- Stress during pregnancy affects the motor, cognitive, and emotional development of the baby.
- The interactive pregnancy education is an interactive approach consisting of three steps that are education about the dangers and prevention of stress in pregnant women, breathing or relaxation techniques and yoga movements, and sharing sessions between pregnant women.
- Interactive pregnancy education method is effective in reducing stress levels and cortisol levels in pregnant women, especially in pregnant women with high levels of stress.

various factors, one of which is the stress experienced by the mother during pregnancy. Stress in pregnant women can be influenced by physiological factors of pregnancy, environment, and hormones.

Stress has consequences throughout the life cycle, which are more severe if it occurs in the early phases of life. Various theories and previous research evidence indicate that high levels of maternal stress during pregnancy are associated with changes in hypothalamic pituitary adrenal (HPA) activity and the placental axis. Increased activity of this system is associated with shorter pregnancies, impaired fetal growth, and factors that place the baby at greater risk for various developmental problems[4,5]. In addition to birth implications, the findings also suggest that

prenatal exposure to stress and stress hormones directly affects fetal central nervous system development. Prenatal experiences can have ongoing implications in later life periods[6].

Research related to stress or anxiety in pregnant women shows that primigravida pregnant women experience more anxiety. Stress in pregnant women often appears in the third-trimester of pregnancy until delivery. This is because the mother feels anxious about her delivery[7–13]. The negative impact arising from the stressful conditions experienced by the mother during the pregnancy period can cause health problems for both the mother and the baby, so efforts are needed to cut the chain of events earlier so that the negative impact on the fetus can be reduced.

One prevention that can be done is the Interactive Pregnancy Education method, also known as the IPE abbreviation, which comprehensively combines approaches to increasing knowledge, emotional, and physical activity. This intervention method is an interactive approach consisting of three steps that are expected to prevent stress during pregnancy. The three steps used in this approach are education about the dangers and prevention of stress in pregnant women, breathing or relaxation techniques and yoga movements, and sharing sessions between pregnant women. The IPE approach is a development of classes for pregnant women, which are held face-to-face at the Community Health Center.

The purpose of this approach is to help pregnant women deal with problems or sources of stress they are experiencing. The education carried out is by providing counseling related to the dangers of stress during pregnancy and how to deal with the stress experienced. Counseling is not carried out in one direction, but the interaction of health workers with pregnant women can be in the form of games, questions and answers, ice-breaking, and so on so that the counseling given is not monotonous. Meanwhile, relaxation techniques and yoga are carried out to provide calm to pregnant women so that negative thoughts related to pregnancy that cause stress can be overcome.

Pregnant women are at risk of experiencing stress. Stress can increase cortisol and epinephrine levels[14]. In this study, each respondent is at risk of experiencing stress during pregnancy, and stress levels will be measured to determine the condition of stress levels at the start of pregnancy. Therefore, with the IPE intervention, the relationship with stress, cortisol, and epinephrine levels will be seen, so that in this study cortisol and epinephrine levels will be used as outcomes.

This study aims to determine the effect of IPE on changes in levels of cortisol, epinephrine, and their relationship with stress levels in primigravida pregnant women in the third-trimester.

Methods

Design

This research is quasi-experimental. This research design has a control group, but cannot fully function to control external variables that affect the implementation of the experiment. This study used a nonequivalent control group design, which has two groups, namely the experimental group and the control group, which were not chosen randomly or deliberately by the researcher.

Population and sample

This research will be carried out in the three Community Health Centers in Indonesia in June-December 2022. The population in this study were all third-trimester primigravida pregnant women who were recorded in the three Community Health Centers in Indonesia. The sampling technique in this study used a purposive sampling technique in which the selection of research subjects was based on several considerations from researchers that were adjusted to the inclusion and exclusion criteria. Taking into account the significance level of 95% or $\alpha = 0.05$ and the power level of 90% or $\beta = 0.10$, $\sigma = 0.78$, and the estimated difference between the mean outcome = 0.65. The selected sample is 60.

Inclusion criteria

(1) Pregnant women with third-trimester primigravida.
(2) Third-trimester primigravida pregnant women who check their pregnancy at the three Community Health Centers in Indonesia.
(3) Pregnant women who are willing to be research respondents.
(4) Pregnant women who do not experience hearing loss.
(5) Pregnant women who can read, write, and communicate well and can speak Indonesian.

Exclusion criteria

- Pregnant women who have diseases such as anemia, cancer, hemochromatosis, hemolytic anemia, leukemia, and infectious diseases such as; HIV/AIDS, malaria, and tuberculosis.
- There is a history of mental disorders before pregnancy.

IPE of pregnant women in the intervention group

The IPE approach is a development of a class for pregnant women, which comprehensively combines approaches to increasing knowledge, emotional, and physical activity in pregnant women to overcome the stress experienced during pregnancy. This intervention is provided by health workers who have been given previous training regarding the IPE method so that they have standardized skills. There are three stages that can be carried out in the IPE approach method, namely: education, breathing relaxation techniques, and yoga movements.

Education is methods provided in the form of counseling regarding the dangers of stress during pregnancy and how to deal with the stress experienced. Counseling is carried out interactively involving the role of health workers and pregnant women using games, questions and answers, and ice-breaking methods. The time required is around 30–40 min.

Breathing relaxation techniques are used to reduce anxiety levels and reduce stress, as well as improve the breathing process in the body. Steps that can be taken in breathing techniques include: 1) the pregnant woman is in a calm condition, 2) inhale through the nose for a count of 3, then hold for 5 to 10 counts, and 3) exhale through the mouth slowly. Apart from these techniques, another alternative to the IPE method of relaxation techniques is mindfulness meditation. This exercise is suitable and safe for pregnant women. Several studies related to meditation show that it is beneficial for people with anxiety, stress or depression, and pain. The steps in this meditation are: 1) the pregnant woman sits comfortably, 2) focuses on breathing, and 3) brings attention and thoughts to the present moment without thinking about the past or future.

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Yoga for pregnant women is a body and mind exercise activity that focuses on flexibility, strength, and breathing, which aims to improve the physical and mental quality of pregnant women. Physical exercise such as prenatal yoga for third-trimester primigravida pregnant women can reduce stress by doing yoga 2 times a week, with a duration of 2 h per meeting, where yoga practice is carried out for 2 weeks. Implementing yoga provides more optimal benefits if accompanied by other activities, namely tai chi, social support, antenatal training, mother and baby workshops, and routine care for pregnant women.

Measurement of cortisol and epinephrine protein levels by ELISA technique

Blood was taken from a vein and centrifuged at 500 rpm to obtain serum. Stored in the freezer until used. The serum was removed from the freezer – 20°C and stored on ice before use. Each sample was duplicated to ensure the validity of the ELISA results. The first stage was the addition of 100 µl Assay Diluent containing protein buffer into each well. Then add 100 µl of standard fluid, which contains the target human cortisol and epinephrine from the predetermined KIT or dilute samples from the patient's serum into each well. Then incubated for 2 h at room temperature. Suck the liquid in each well and wash with sterile PBS. This washing process was carried out four times in succession. Then 200 µl of conjugate liquid containing streptavidin HRP was added to each well/well and covered with a plastic cover and incubated for 2 h at room temperature. The liquid was sucked in and then washed again four times using sterile PBS. In the next process, 200 µl substrate solution containing TMB was added to each well and read using an ELISA Reader 270 (Biomerieux)[15–20].

Procedure

This study compared the experimental group that was given the intervention with the control group that was not given any treatment. Both the experimental group and the control group were given a pretest and then the results were sought. After that, the experimental group received treatment while the control group did not receive treatment. Then both were given a post-test to find out the results of the treatment that had been carried out. The research flow is described in Figure 1.

Data analysis

Data analysis is done by entering and processing data into the computer. Then the data were analyzed using computerization through the SPSS program. A univariate analysis was conducted to see the median (middle value), mean (average), SD, and frequency distribution of each variable. This analysis was carried out to describe the research variables by making a frequency distribution table and data distribution in tabular form. The purpose of this analysis is to explain the characteristics of each of the variables studied. The data displayed in the univariate analysis are the frequency distribution of the characteristics of pregnant women, knowledge about stress in pregnancy, and adherence to attending classes for pregnant women.

While the bivariate analysis was performed to determine the correlation between the independent variables and the dependent variable using the χ^2 test at α 0.05 with a 95% degree of confidence. If the *P*-value <0.05 means that the statistical calculation is significant (significant) or indicates a relationship between the two variables. Dependent *t*-test or paired *t*-test, which was conducted to test the mean difference between the two dependent data groups before and after the IPE intervention was given. The selection of this test was carried out if it met the normal distribution requirements and the types of numerical and categorical variables in the two groups. If the *P*-value <0.05 means that the statistical calculation is significant (significant) or indicates a relationship between the two variables. However, if the data normality test shows that the data is not normally distributed, a nonparametric statistical test will be performed using Mann–Whitney. Confounding factors such as age, education, occupation, income, husband's support and family has been controlled in this study.

The Figure 1 above illustrates the research flow, starting from the sample collection process, physical examination, questionnaire completion, pretest measurements (stress levels assessment, cortisol, and epinephrine examination), the administration of IPE intervention in the intervention group, post-test measurements (stress levels assessment, cortisol, and epinephrine examination), followed by the data analysis stage and research results.

Results

Univariate analysis of the results of this study explains the descriptive statistics shown by the table of the characteristics of the research subjects. From the result in Table 1, the proportion of the control group was 50% ($n = 30$) and the intervention group was 50% ($n = 30$). The median value for cortisol was 25.14 (12.25–575.47) pg/ml and the median value for epinephrine was 20.22 (12.00–116.60) pg/ml. The median stress level is 11.5 (1–40) with a normal stress level proportion of 61.7% ($n = 37$), not normal 38.3% ($n = 23$). The median age of the study subjects was 25 (17–38) years with the proportion of age less than 21 years 8.3% ($n = 5$), age 20–34 years 81.7% ($n = 49$), age greater than or equal to 35 years 10.0% ($n = 6$). The proportion of higher education is 25% ($n = 15$), and low education is 75% ($n = 45$). The proportion of housewives is 93.3% ($n = 56$), and employees/professionals are 6.7% ($n = 4$). The proportion of income greater than 4 million 50% ($n = 30$), less than or equal to 4 million 50% ($n = 50$). The median gestational age was 29 (24–35) weeks with the proportion of gestational age 24–29 weeks 63.3% ($n = 38$), and gestational age 30–35 weeks 36.7% ($n = 22$). The proportion of no family dysfunction was 83.3% ($n = 50$), moderate family dysfunction was 15% ($n = 9$), and high family dysfunction was 1.7% ($n = 1$).

Differences in the characteristics of research subjects based on the control group and the intervention group

The result in Table 2 shows that in the control group, the median value for cortisol was 22.28 (12.25–575.47) pg/ml and the median value for epinephrine was 30.99 (12.86–116.60) pg/ml. The median stress level was 8 (1–30) with a normal stress level proportion of 66.7% ($n = 20$), 33.3% ($n = 10$) abnormal. The median age of the subjects was 26 (17–38) years with the proportion of age less than 21 years 10% ($n = 3$), age 20–34 years 70% ($n = 21$), age greater than or equal to 35 years 20.0% ($n = 6$). The proportion of higher education is 13.3% ($n = 4$), and low education is 86.7% ($n = 26$). The proportion of housewives is 96.7% ($n = 29$), and employees/professionals are 3.3% ($n = 1$). The proportion of income greater than 4 million is 40% ($n = 12$),
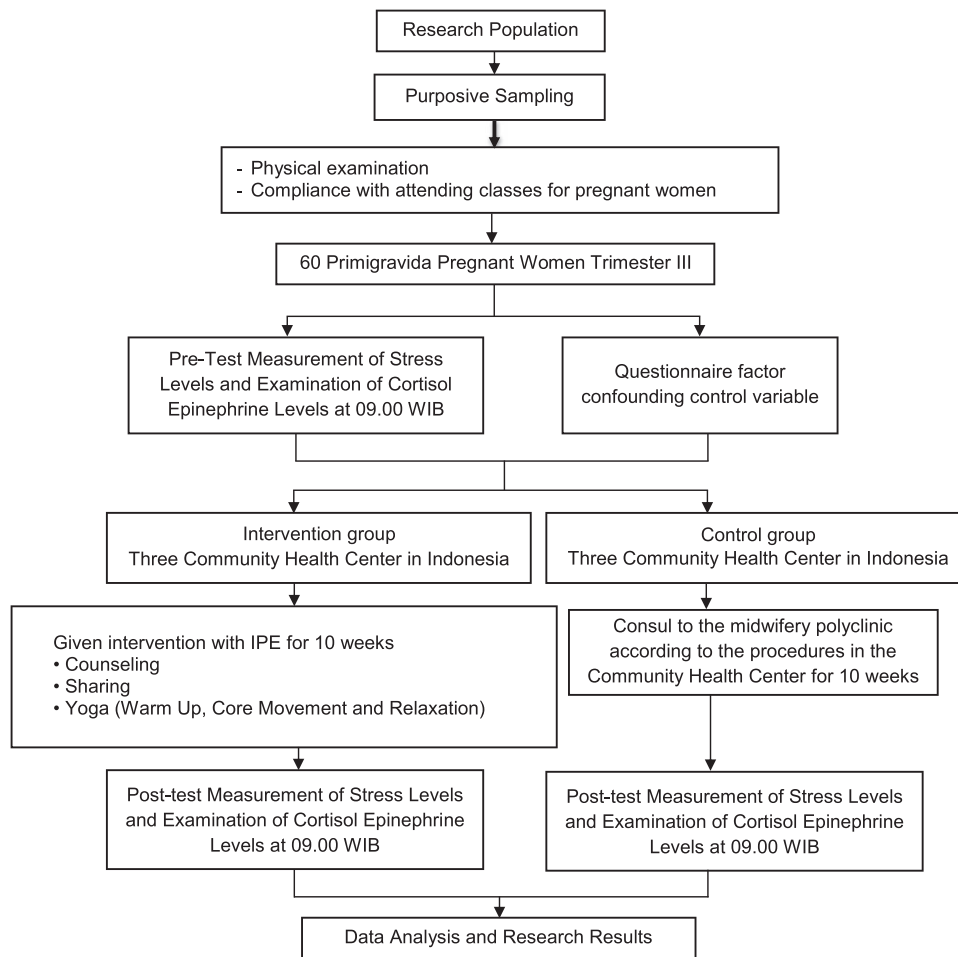
Figure 1. Research flow.

less than or equal to 4 million is 60% ($n = 18$). The median gestational age was 28 (27–33) weeks with the proportion of gestational age 24–29 weeks 76.7% ($n = 23$), and gestational age 30–35 weeks 23.3% ($n = 17$). The proportion of no family dysfunction was 90.0% ($n = 27$), moderate family dysfunction was 10% ($n = 3$), and high family dysfunction was 0.0% ($n = 0$).

In the control group, the median value for cortisol was 27.15 (14.75–396.01) pg/ml and the median value for epinephrine was 18.62 (12–59.35) pg/ml. The median stress level was 12.5 (3–40) with a normal stress level proportion of 56.7% ($n = 17$), 43.3% ($n = 13$) abnormal. The median age of the subjects was 24.50 (19–31) years with the proportion of age less than 21 years 6.7% ($n = 2$), age 20–34 years 93.3% ($n = 28$), age greater than or equal to 35 years 0, 0% ($n = 0$). The proportion of higher education is 36.7% ($n = 11$), and low education is 63.3% ($n = 19$). The proportion of IRT jobs is 90% ($n = 27$), and employees/professionals 10% ($n = 3$). The proportion of income greater than 4 million is 60% ($n = 15$), and less than or equal to 4 million is 40% ($n = 12$). The median gestational age was 29.50 (24–35) weeks with the proportion of gestational age 24–29 weeks 50% ($n = 15$), gestational age 30–35 weeks 50% ($n = 15$). The proportion of no family dysfunction was 76.7% ($n = 23$), moderate family dysfunction was 20% ($n = 6$), and high family dysfunction was 3.3% ($n = 1$).

The relationship between the characteristics of research subjects and stress levels, cortisol levels, and epinephrine levels

Bivariate analysis was carried out to see the relationship between the characteristics of the research subjects on stress levels, cortisol levels, and epinephrine levels. This analysis uses the χ^2 test and Mann–Whitney test. The results of the analysis of Table 3 show that the potential variables for stress levels are the mother's age (OR: 2.2; 95% CI: 0.6–8.5; $P = 0.306$), education (OR: 2.0; 95% CI: 0.5–7.3; $P = 0.366$), occupation (OR: 1.9; 95% CI: 0.2–19.9; $P = 1.000$), income (OR: 1.5; 95% CI: 0.5–4.4; $P = 0.596$), gestational age (OR: 2.9; 95% CI: 1.0–8.8; $P = 0.060$), family support (OR: 2.9; 95% CI: 0.7–11.7; $P = 0.160$). Subject characteristics related to cortisol levels were family support with a P-value of 0.034. Meanwhile, the characteristics of the study subjects related to epinephrine levels were income (P-value 0.018) and gestational age (P-value 0.035).

Interaction test of research subject characteristics with cortisol levels and epinephrine levels

The interaction test aims to determine the interaction between the independent variable and the dependent variable using the

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Table 1

Distribution of frequency characteristics of research subjects (*n* = 60)

Variable	*n*	%
IPE (Interactive Pregnancy Education)		
Control	30	50.0
Intervention	30	50.0
Cortisol level median (min-max)	25.14	12.25–575.47
Epinephrine level median (min-max)	20.22	12.00–116.60
Stress level Median (min-max)	11.5	1–40
Normal	37	61.7
Not normal	23	38.3
Age median (min-max)	25	17–38
< 21 years	5	8.3
21–34 years	49	81.7
≥ 35 years	6	10.0
Education		
High (Diploma – University)	15	25.0
Low (Elementary, Junior, and Senior High School)	45	75.0
Occupation		
Housewife	56	93.3
Employee/Professional	4	6.7
Income		
> 4.000.000 IDR	30	50.0
≤ 4.000.000 IDR	30	50.0
Maternal Age (min-max)	29	24–35
24–29 weeks	38	63.3
30–35 weeks	22	36.7
Family support		
No family dysfunction	50	83.3
Moderate family dysfunction	9	15.0
High family dysfunction	1	1.7

ng/ml cortisol and epinephrine.
Primary data source.
IDR, Indonesian Rupiah.

Table 2

Distribution of frequency characteristics of research subjects based on control (*N* = 30) and intervention groups (*N* = 30)

	Control		Intervention	
Variable	*n*	%	*n*	%
Cortisol levels median (min-max)	22.28	12.25–575.47	27.15	14.75–396.01
Epinephrine levels median (min-max)	30.99	12.86–116.60	18.62	12.00–59.35
Stress Levels Median (min-max)	8	1–30	12.50	3–40
Normal	20	66.7	17	56.7
Not normal	10	33.3	13	43.3
Age median (min-max)	26	17–38	24.50	19–31
< 20 years	3	10.0	2	6.7
20–34 years	21	70.0	28	93.3
≥ 35 years	6	20.0	0	0.0
Education				
High	4	13.3	11	36.7
Low	26	86.7	19	63.3
Occupation				
Housewife	29	96.7	27	90.0
Employee/Professional	1	3.3	3	10.0
Income				
> 4.000.000 IDR	12	40.0	18	60.0
≤ 4.000.000 IDR	18	60.0	12	40.0
Gestational Age median (min-max)	28	27–33	29.50	24–35
24–29 weeks	23	76.7	15	50.0
30–35 weeks	17	23.3	15	50.0
Family support				
No family dysfunction	27	90.0	23	76.7
Moderate family dysfunction	3	10.0	6	20.0
High family dysfunction	0	0.0	1	3.3

ng/ml cortisol and epinephrine.
IDR, Indonesian Rupiah.

General Linear Model (GLM) test. The results of the interaction test analysis are as follows:

Social determinants (education and employment)

The analysis in Table 4 shows that there is no interaction between education and work variables with cortisol levels (F value = 0.016 and *P*-value = 0.900) with a negative relationship (adjusted R2 – 0.045) and very weak relationship strength (R2 0.008). Meanwhile, at epinephrine levels, there was an interaction between education and work variables (F value = 0.163 and *P*-value = 0.688) but had a negative relationship (adjusted R2 – 0.048) and very weak relationship strength (R2 0.006). The interaction can also be seen in the line pieces. If there is a line cut, it can be said that there is an interaction. From the results of the analysis, it can be seen that there is no interaction between education and work with cortisol levels, whereas there is an interaction with epinephrine.

Cortisol levels can only be explained by the variables of work and education 0.8%, most (100–0.8% = 99.2%) can be explained by other factors not examined in this study. While epinephrine levels can only be explained by the variables of work and education 0.6%, most (100–0.6% = 99.4%) can be explained by other factors not examined in this study.

Social determinants (income and family support)

Table 5 shows that there is an interaction between income and family support variables with cortisol levels (F value = 5.293 and *P*-value ≤ 0.001) with a positive relationship (adjusted R2 0.709) and very strong relationship strength (R2 0.882) and levels of epinephrine (F value = 0.534 and *P*-value = 0.880) but has a negative direction (adjusted R2 – 0.328) and weak relationship strength (R2 0.460). From the results of the analysis, it appears that there is a cut line between income and family support with cortisol and epinephrine levels. This means that there is an interaction between income and family support with cortisol and epinephrine.

Cortisol levels can be explained by income and family support variables 88.2%, the rest (100–88.2% = 11.8%) is explained by other factors not examined. Meanwhile, epinephrine levels can be explained by income and family support variables 46%, and some (100–46% = 54%) are explained by other factors that were not present in this study.

Maternal factors (age and age of pregnancy)

The results of Table 6 show that there is an interaction between the variables of age and gestational age of the mother with cortisol levels (F value = 124.783 and *P*-value ≤ 0.001) and epinephrine levels (F value = 2.219 and *P*-value = 0.081) with a positive relationship (adjusted R2 0.988 for cortisol and 0.635 for epinephrine) with very strong relationship strengths (cortisol

Table 3

Relationship between the characteristics of the research subjects on stress scores, cortisol levels, and epinephrine levels ($N = 60$)

Characteristics	Stress levels						Cortisol levels		Epinephrine levels	
	Normal		Not normal							
	n	%	n	%	P	OR (95% CI)	Mean ± SD	P	Mean ± SD	P
Age										
No risk	32	65.3	17	34.7	0.306	1,0 (ref.)	54.08 ± 101.9	0.218	25.88 ± 18.1	0.178
Risk	5	45.5	6	54.5		2,2 (0,6 – 8,5)	72.44 ± 93.5		31.47 ± 15.9	
Education										
High	11	73.3	4	26.7	0.366	1,0 (ref.)	48.32 ± 71.7	0.458	25.48 ± 18.8	0.235
Low	26	57.8	19	42.2		2.0 (0,5 – 7,3)	60.48 ± 108.3		27.38 ± 17.5	
Occupation										
Employee	3	75.0	1	20.0	1.000	1.0 (ref.)	27.13 ± 4.0	0.657	27.54 ± 7.7	0.441
Housewife	34	60.7	22	39.3		1.9 (0.2–19.9)	59.61 ± 103.1		26.86 ± 18.3	
Income										
>Rp. 4.000.000	20	66.7	10	33.3	0.596	1.0 (ref.)	49.22 ± 83.3	0.198	23.12 ± 14.1	0.018[a]
≤RP. 4.000.000	17	56.7	13	43.3		1.5 (0.5 – 4.4)	65.66 ± 115.0		30.70 ± 20.2	
Gestational age										
24–29 weeks	27	71.1	11	28.9	0.060	1.0 (ref.)	44.16 ± 61.6	0.390	28.73 ± 18.0	0.035[a]
30–35 weeks	10	45.5	12	54.5		2.9 (1.0 – 8.8)	80.36 ± 143.2		23.75 ± 17.3	
Family support										
No family disfunction	33	66.0	17	34.3	0.160	1.0 (ref.)	35.95 ± 44.0	0.034[a]	27.14 ± 18.5	0.851
Family disfunction	4	40.00	6	60.0		2.9 (0.7–11.7)	164.92 ± 198.7		27.14 ± 18.5	

[a]Mann–Whitney test, P-value <0.05.
OR, odd ratio.

(R2 0.998) and epinephrine (R2 0.926)). From the results of the analysis, it appears that there is a cut line between maternal age and gestational age with cortisol and epinephrine levels. This means that there is an interaction between maternal age and gestational age with cortisol and epinephrine levels.

Cortisol levels can only be explained by age and gestational age variables 99.8%, the rest (100–99.8% = 0.2%) can be explained by other factors not examined in this study. While epinephrine levels can be explained by age and gestational age variables 92.6%, the rest (100–92.6% = 7.4%) can be explained by other factors not examined in this study.

Correlation of stress levels with cortisol levels and epinephrine levels

Based on the results of the analysis in Table 7, it can be seen that the correlation between stress levels and cortisol levels has a positive and strong relationship. That is, if the cortisol level increases, the respondent's stress level also increases. Cortisol levels can explain a 53.4% variation in stress levels. While the stress level with epinephrine levels has a positive relationship

Table 4

Interaction of education and work variables with cortisol levels and epinephrine levels

Variables	R Squared	Adjusted R Squared	F	P
Education * Occupation				
Cortisol	0.008	− 0.045	0.016	0.900
Epinephrine	0.006	− 0.048	0.163	0.688

General Linear Model (GLM) test.
R2 or R Squared, coefficient of determination.
F, simultaneous test.

direction but has a very weak strength. Epinephrine levels can explain a 5.6% variation in stress levels.

Differences in stress levels, cortisol levels, and epinephrine levels before and after intervention based on the control and intervention groups

Based on Table 8, which shows before and after the intervention, the reduction in stress levels was statistically significant at $\alpha = 0.05$ (P-value ≤ 0.001). There was a decrease in cortisol levels before and after the intervention. The decrease in cortisol levels was not statistically significant at $\alpha = 0.05$ (P-value = 0.072). There was no decrease in epinephrine levels before and after the intervention. Epinephrine levels were not statistically significant at $\alpha = 0.05$ (P-value = 0.082).

Relationship of stress levels to cortisol and epinephrine before and after IPE intervention

The results of statistical analysis on the relationship between stress levels and epinephrine levels both before and after the intervention showed that there was a significant relationship between maternal stress levels and cortisol levels (P-value <0.005) in both the control and IPE intervention groups (Table 9). Meanwhile, for epinephrine levels in both the control group and the intervention group, there was no relationship between stress levels and epinephrine levels (P-value > 0.005). However, after the IPE intervention, the stress level on epinephrine levels had a significant relationship (P-value <0.005). To be clearer, the statistical results of the relationship between stress levels and levels of cortisol and epinephrine can be seen in Table 9 below.

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Table 5

Interaction of income and family support variables with cortisol levels and epinephrine levels

Variables	R Squared	Adjusted R Squared	F	P
Income * Family support				
Cortisol	0.882	0.709	5.293	< 0.001
Epinephrine	0.460	-0.328	0.534	0.880

General Linear Model (GLM) test.
R2 or R Squared, coefficient of determination.
F, simultaneous test.

Discussion

The results of this study indicate that IPE has a good impact on pregnant women, where there is a significant relationship in the post-test in the intervention group. This indicates that IPE contributed to the difference in post-test scores in the intervention group. Similar results were shown by research conducted by Gandomi *et al.* (2022), which showed educational interventions reduced maternal anxiety and stress levels. In practice, IPE interventions can reduce the fear of giving birth to children with physical or psychological problems, fear of mood swings, and so on[21].

Psychological stress during pregnancy is an important phenomenon that is unfortunately not measured in routine pregnancy care, so the extent of stress during pregnancy and its impact on maternal health. On the other hand, aggressive measures to assess the health of the fetus can increase the psychological pressure on pregnant women. Mojahed *et al.*[22] revealed that individual and group counseling and educational methods are effective in reducing stress and anxiety during pregnancy.

The knowledge of pregnant women, especially primigravida mothers, is very important because they have not had previous experience with pregnancy and childbirth. This is different from a mother who has experienced pregnancy and childbirth before, who will certainly know what she needs to prepare for, including mentally, so that her stress and anxiety about childbirth are reduced. Mothers with high knowledge and working in the formal sector will be more independent in determining attitudes and treatment actions because they receive health information[23,24]. One inexpensive and effective strategy to promote pregnant women's perceived self-efficacy and reduce stress levels during pregnancy is to design and implement different educational interventions[25].

The general understanding of the mother has an impact on the health of the mother's fetus. The less knowledge the mother has the less desire to use health services. There are still other factors

that can affect anxiety besides knowledge. Regarding research on the level of anxiety of primigravida mothers facing childbirth in terms of maternal age and socioeconomic factors. When mothers aged 20–35 experience pregnancy, this is considered safe, and in dealing with anxiety, mothers can also control it[26].

The IPE approach is a method specifically used for pregnant women to deal with the stress experienced during pregnancy. This approach is the development of a class for pregnant women that comprehensively combines approaches to increase knowledge, emotional, and physical activity in pregnant women. The results showed that there were differences in cortisol levels before and after IPE. This research is not in line with research conducted by Kumorojati *et al.*[27] who intervened in yoga movements in pregnant women and found that there was a significant effect after the intervention of yoga movements on changes in cortisol levels in pregnant women.

Theoretically, cortisol is a very important regulator in humans, free cortisol in the blood has a negative feedback on the release of corticotrophin-releasing hormone (CRH) from the hypothalamus. CRH will descend through the veins of the hypothalamic portal system to the anterior pituitary and stimulate the release of ACTH (adrenocorticotropic hormone). There will be an increase in cortisol levels when someone experiences psychological stress[28].

In normal pregnancy, the hormone cortisol will increase two to four times the normal adult cortisol levels (Su *et al.*, 2015). Pregnant women are sensitive to hypothalamic-pituitary-adrenal (HPA) axis dysregulation; which secretes cortisol due to hormonal changes during pregnancy. The hormone cortisol is released in response to stress and is a major physiological marker

Table 6

Interaction of age and gestational age variables with cortisol levels and epinephrine levels

Variables	R Squared	Adjusted R Squared	F	P
Maternal age				
Cortisol	0.998	0.988	124.783	< 0.001
Gestational age				
Epinephrine	0.926	0.635	2.219	0.081

General Linear Model (GLM) test.
R2 or R Squared, coefficient of determination.
F, simultaneous test.

Table 7

Correlation of stress levels with cortisol levels and epinephrine levels ($N = 60$)

	R	R square (R^2)	P
Stress levels			
Cortisol	0.731	0.534	< 0.001
Epinephrine	0.237	0.056	0.068

Spearman Correlation test.
R2 or R Squared, coefficient of determination.

Table 8

Differences in stress levels, cortisol levels, and epinephrine levels before and after intervention based on the control and intervention groups

Variable	Control ($N = 30$)			Intervention ($N = 30$)		
	Mean	SD	P	Mean	SD	P
Stress levels						
Pretest	10.8	8.4	0.295	14.2	9.3	< 0.001
Post-test	11.8	7.3		7.4	6.0	
Cortisol levels						
Pretest	54.7	110.2	0.210	60.2	90.2	0.072
Post-test	29.7	8.9		31.9	12.1	
Epinephrine levels						
Pretest	32.5	22.0	0.540	21.2	9.4	0.089
Post-test	30.1	9.5		24.4	9.3	

Wilcoxon test.

Table 9

Relationship of stress levels to cortisol levels and epinephrine levels before and after intervention (N = 30)

Stress Levels	Control				Intervention			
	Cortisol		Epinephrine		Cortisol		Epinephrine	
	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P	Mean ± SD	P
Before								
Normal	19.59 ± 5.63	< 0.001[a]	28.35 ± 16.87	0.147	21.02 ± 4.80	< 0.001[a]	19.07 ± 5.78	0.116
Not normal	124.95 ± 175.68		40.96 ± 29.13		111.37 ± 120.98		24.12 ± 12.35	
After								
Normal	25.39 ± 6.19	0.002[a]	24.45 ± 7.56	0.001[a]	29.40 ± 10.65	0.003[a]	21.87 ± 7.14	0.002[a]
Not normal	34.06 ± 9.23		35.78 ± 7.90		48.46 ± 7.40		40.70 ± 2.69	

[a]Mann–Whitney test.

of activation of the stress response. Stressors experienced by pregnant women will stimulate the HPA axis by releasing corticosteroids, which have an effect on reducing immune function[29].

One of the IPE approach methods used is an emotional approach and physical activity through relaxation and yoga exercises. A study conducted by Weissgerber, et al.[30] showed that fetuses born to mothers who exercised diligently tolerated labor better than fetuses from mothers who did not exercise. The IPE approach during pregnancy improves the birth weight, reduces preterm labor, and decreases intrauterine growth retardation either in isolation or associated with pre-eclampsia, without increasing complications[31]. In addition, routinely implementing yoga movements in the IPE approach has also been shown to reduce inflammatory markers, lower heart rate, and produce improvements in physical fitness variables, all of which can work together with changes in behavior and psychosocial functioning to increase reactivity to stress and pain[32].

Stress that occurs due to various psychosocial stressors during pregnancy can affect biochemical and physiological adaptations to optimally support pregnant women's health, as well as prenatal and postnatal growth and development[33,34]. This suggests that relaxation interventions can help pregnant women maintain or adjust normal homeostasis. Relaxation improves breathing and helps the body release muscle tension and regain calm and a sense of rest by increasing heart rate, blood pressure, digestion, absorption, and blood circulation[35,36]. Through this mechanism, relaxation helps reverse the development or worsening of symptoms of anxiety and depression in pregnant women, one of which is relaxation in the IPE approach.

In addition to cortisol levels, another aspect that was examined was epinephrine levels, and the results showed that there was no decrease in epinephrine levels after the IPE intervention. This result is in line with a study conducted by Henrique et al.[37], which showed similar results, namely that there was no significant difference in epinephrine levels after nonpharmacological interventions. Studies by Hux, Watkins, Blumenthal, Cohen, and Sherwood show that anxiety is related to the autonomic nervous system and increased mortality through cardiovascular disorders[38]. Renard et al.[39] also stated that catecholamines such as epinephrine and nor-epinephrine increase conditions of stress and anxiety.

Studies by Cameron et al.[40], White and Depao, and Azorat also confirmed a significant increase in nor-epinephrine and changes in the performance of the noradrenergic system in anxiety disorders. The study by Hux also demonstrated an increase in 24 h urinary nor-epinephrine metabolites in patients with anxiety[38]. Another study by Ayala demonstrated increases in certain neurotransmitters in anxiety and social phobia, and also that the no-adrenaline response alters the timing of anxiety states, and that there is a reduction in postsynoptic α-2 adrenergic receptors along with an increase in nor-epinephrine activity in anxiety. According to their study, it was identified that social isolation in monkeys causes an increase in nor-epinephrine in the cerebrospinal fluid[41]. In addition, Renard's studies demonstrated that in male and female rats, maternal separation causes chronic anxiety and affects central adrenal gland response, and sex changes in epinephrine and nor-epinephrine levels[39]. Mothers with various degrees of stress are at risk of causing abortion and other disorders of fetal growth and development, which cause fetal abortion, premature births, and low birth weight (LBW). The IPE approach is a method specifically used for pregnant women to deal with the stress experienced during pregnancy[42].

Limitations of the study

This research was conducted to determine the effect of IPE on changes in cortisol levels, epinephrine, and their relationship with stress levels in primigravid trimester III pregnant women. The number of primigravida pregnant women in their third-trimester at the study site was very limited, and some respondents dropped out during the study for several reasons the researchers could not control. Confounding factors that can influence cortisol/epinephrine such as eating patterns, sleep, exercise outside the intervention were not controlled due to limited research time. Other factors that could affect cortisol and epinephrine levels in pregnant women during the study were not controlled by the researchers, causing a high bias in the research and the results of data analysis. The results of studies regarding cortisol still show inconsistencies with previous studies. Therefore, further scientific evidence is still needed regarding the relationship between IPE, stress, and cortisol levels in pregnant women.

Conclusion

In the intervention group, there was a decrease in stress levels and cortisol levels before and after the IPE intervention. Whereas there was no decrease in epinephrine levels before and after the IPE intervention. There is a significant relationship between stress

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levels and cortisol levels both before and after the IPE intervention. Meanwhile, on epinephrine levels, there was no relationship between stress levels of pregnant women and epinephrine levels before the intervention, but after the IPE intervention, there was a significant relationship. The IPE method is effective in reducing stress levels and cortisol levels in pregnant women, especially in pregnant women with high levels of stress. However, IPE is not effective in reducing epinephrine levels in pregnant women.

There needs to be an encouragement to increase family participation in providing support both materially and morally to pregnant women so they can maintain the health of the fetus and themselves during pregnancy. Further research is needed regarding the level of stress in pregnant women and their experience in carrying out IPE both in primigravids and in multigravidas as well as other factors that can affect stress levels in pregnant women.

Ethical approval and consent to participants

This research has received recommendations for ethical approval from the health research ethics committee of Universitas Hasanuddin Makassar with number 292/UN4.6.4.5.31/PP36/2022.

Consent

Written informed consent was obtained from the patients for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

E.H., S.R., M.H., and S.T.L.: concept or design; E.H., J.J.W., S.S., M.T.C.: data collection; E.H., A.S., A.A.Z., H.M.D., F.M.T., H.P.S.: data analysis; E.H., T.A.E.P., and N.L.: writing the paper.

Conflicts of interest disclosure

Author have no conflicts of interest to declare.

Registration of research studies

(1) Name of the registry: Interactive Pregnancy Education (IPE) on Stress, Cortisol, and Epinephrine Level in Primigravida of Trimester III Pregnant: A Quasi-Experimental.
(2) Unique identifying number or registration ID: researchregistry 9391.
(3) Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/register-now#user-researchregistry/registerresearchdetails/64d5c2570d5c6e00291270a8/.

Guarantor

Elli Hidayati, Syahrul Rauf, and Mochammad Hatta.

Data availability statement

Elli Hidayati, SST., and MKM.

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