

## Common mental disorders increase pre-eclampsia/ eclampsia risks in pregnancy

Y. Wibowo\*, M Hakimi\*\*, and C.R Marchira\*\*\*

### ABSTRACT

\*Department of Public Health  
and Community Medicine,  
Medical Faculty, Jenderal  
Soedirman University

\*\*Department of Obstetrics  
and Gynecology, Faculty of  
Medicine,

Gadjah Mada University

\*\*\*Department of Psychiatry,  
Faculty of Medicine,

Gadjah Mada University

#### Correspondence

dr. Yudhi Wibowo

\*Department of Public Health  
and Community Medicine,  
Medical Faculty, Jenderal  
Soedirman University

Phone:

Email :

dr\_yudhi\_wibowo@yahoo.com

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#### INTRODUCTION

Pre-eclampsia is a multisystem complication that occurs after 20 weeks of pregnancy and can cause considerable maternal and fetal morbidity and mortality. Mental health is influenced by social support, and emotional distress during pregnancy may cause pre-eclampsia/eclampsia (PE/E). The objective of this study was to determine the association of social support and common mental disorders (CMD) with PE/E in pregnant women.

#### METHODS

This study was a matched case-control study. Cases were pregnant women who had been diagnosed with PE/E. Controls were those with normal pregnancies or not diagnosed as PE/E. Instruments social support questionnaire-6 (SSQ-6) was used to measure social support and self-reporting questionnaire 20 (SRQ-20) items for measuring CMD. Conditional logistic regression was used to estimate matched odds ratios (ORs) and 95% confidence intervals (95% CI).

#### RESULTS

Low social support was not directly associated with PE/E. Compared with women with high social support, those with low social support had a 26-fold increased risk of CMD (+) (OR=26.4, 95% CI: 10.67 to 77.20, p=0.001). Several variables significantly associated with PE/E were CMD (+) (OR=6.11, 95% CI: 2.99 to 14.07, p=0.001), low family income (OR=2.93, 95% CI: 1.56 to 5.82, p=0.001), history of chronic hypertension (+) (OR=7.67, 95% CI: 2.32 to 39.89, p=0.001), history of PE/E (+) (p=0.001), and history of hereditary PE/E (+) (OR=6, 95% CI: 1.34 to 55.20, p=0.013).

#### CONCLUSION

Low social support was not directly associated with PE/E but was associated with CMD. To prevent CMD in pregnant women, there is a need for social support from the family.

**Key words:** Social support, common mental disorders, preeclampsia, eclampsia, pregnancy

## Gangguan jiwa ringan meningkatkan risiko dengan pre-eklampsia/eklampsia pada ibu hamil

### ABSTRAK

#### PENDAHULUAN

Pre-eklampsia merupakan komplikasi multisistem yang terjadi setelah kehamilan 20 minggu dan dapat menimbulkan tingkat morbiditas dan mortalitas maternal dan fetal. Dukungan sosial mempengaruhi kesehatan mental maka distress selama kehamilan kemungkinan mengarah kepada pre-eklampsia/eklampsia (PE/E). Tujuan penelitian ini adalah untuk menganalisis hubungan dukungan sosial dan gangguan jiwa ringan (CMD) pada ibu hamil dengan PE/E.

#### METODE

Penelitian ini merupakan matched case-control. Kasus adalah ibu hamil yang telah didiagnosis PE/E. Kontrol adalah ibu dengan kehamilan normal atau tidak didiagnosis sebagai PE/E. Instrumen penelitian adalah social support questionnaire-6 (SSQ-6) yang digunakan untuk mengukur dukungan sosial and self-reporting questionnaire-20 (SRQ-20) untuk mengukur CMD. Kondisional regresi logistik digunakan untuk mengestimasi matched Odds Ratio (OR) dan Confidence Interval 95% (CI 95%).

#### HASIL

Dukungan sosial yang rendah tidak berhubungan langsung dengan PE/E. Dibandingkan dengan kelompok dukungan sosial tinggi, kelompok dukungan sosial rendah memiliki 26 kali peningkatan risiko gangguan jiwa ringan (CMD +) (OR=26,4, 95% CI: 10,67 to 77,20, p=0,001). Variabel yang berhubungan signifikan dengan kejadian PE/E adalah CMD (+) (OR=6,11, 95% CI: 2,99 to 14,07, p=0,001), pendapatan keluarga rendah (OR=2,93, 95% CI: 1,56 to 5,82, p=0,001), riwayat hipertensi kronik (+) (OR=7,67, 95% CI: 2,32 to 39,89, p=0,001), riwayat PE/E (+) (p=0,001), dan riwayat keturunan PE/E (+) (OR=6, 95% CI: 1,34 to 55,20, p=0,013).

#### KESIMPULAN

Dukungan sosial rendah tidak berhubungan langsung dengan PE/E akan tetapi berhubungan dengan CMD. Untuk pencegahan CMD pada kehamilan diperlukan dukungan sosial dari keluarga.

**Kata Kunci:** Dukungan sosial, gangguan jiwa ringan, preeklampsia, eklampsia, kehamilan

## INTRODUCTION

The maternal mortality rate (MMR) in Indonesia of 228/100000 live births (LB) is higher than in other ASEAN countries.<sup>(1)</sup> In Sukoharjo district in 2010, MMR of 152.28/100000 LB was over the national target of 117.1/100000 LB. The direct cause of maternal death is the high pre-eclampsia/eclampsia (PE/E) (47.62%) and since the years 2007-2011, PE/E has been the direct cause of the highest maternal mortality rate. PE is a multi-systemic syndrome usually recognized

by new-onset hypertension and proteinuria in the second half of pregnancy.<sup>(2,3)</sup> Common mental disorders (CMD) in pregnancy are depressive and anxiety disorders that are classified in ICD-10 as “neurotic, stress-related and somatoform disorders” and “mood disorders”.<sup>(4,5)</sup> Distress conditions (depression, anxiety and stress) during pregnancy can induce PE.<sup>(6)</sup> Family structure modifies the association but, contrary to expectations, spousal emotional support is a stronger correlate of antenatal depression in traditional rather than nuclear family settings.<sup>(7)</sup>

Depression and anxiety in early pregnancy are associated with a 2.5 and 3.2-fold risk, respectively, for subsequent PE. Mental stress is frequently associated with PE.<sup>(8)</sup> The World Health Organization has estimated that the prevalence of mental disorders in pregnant women in low-to-middle income countries is 10-41.2%.<sup>(9)</sup> In Brazil, prevalence of CMD in pregnant women in low social economic is 20.2%.<sup>(10)</sup> The prevalence of mental emotional disorders in Indonesia's population aged >15 years is 11.6%.<sup>(11)</sup> Chronic hypertension is an independent risk factor for severe preeclampsia.<sup>(12)</sup> Subjects living alone or as couples are significantly more likely to suffer from severe hypertension in comparison to those living in extended families.<sup>(13)</sup> Sukoharjo District was the 4<sup>th</sup> district with a high prevalence of primary hypertension of 10.89%.<sup>(14)</sup> A particularly important potential consequence of global population expansion and trans-national and rural-urban migration has been the disruption of traditional family-based support structures.

The association between social support, psychological stress and pregnancy outcome is undoubtedly complex. The importance and implications of social support during pregnancy remain incompletely understood.<sup>(15)</sup> Therefore this study was conducted to analyze the association of social support and CMD with PE/E in pregnancy.

## METHODS

### Research design

This study was a facility-based matched case-control study in Sukoharjo District, conducted from January 2010-December 2011.

### Study subjects

Cases were pregnant women who had been diagnosed as having PE/E by hospital doctors (blood pressure  $\geq$ 140/90 mmHg, with proteinuria and or seizures). Controls were pregnant women with normal pregnancies or not diagnosed as PE/E by health personnel (doctors, midwives or

nurses) in primary health care, based on medical records (MR), register cohort of mothers and maternal & child health (MCH) book. Cases and controls were matched on maternal age and parity. Calculation of the sample size was based on the results of previous studies and odds ratio (OR) discordant proportion ( $\delta$ ) =0.4, using 95% confidence level with  $\alpha$  =5%, power (1- $\hat{\alpha}$ ) =80% and OR gained 2.0 to 3.2; at least 82 respondents for both case and control groups.<sup>(16)</sup>

### Measurements

For interview of participants a structured questionnaire was used, comprising items on age, family structure, parity, inter-pregnancy interval, history of antenatal care (ANC), history of contraception used, history of abortion, history of PE/E, history of hereditary PE/E, and history of chronic hypertension. Total family income is the income of all family members per month, and high if higher than or equal to the minimum regional salary.

The social support questionnaire-6 (SSQ-6) is one's perception that he endeared, appreciated and be a part community, and a score is considered high if it is higher than or equal to the median value. The validity of the SSQ-6 in Indonesia for measuring social support has been tested, as has been the validity of self-reporting questionnaire 20 items (SRQ-20) to measure common mental disorders (CMD).<sup>(17,18)</sup> The SRQ-20 consists of twenty questions, which have to be answered by 'yes' (1) or 'no' (0). Item scores are summarized to obtain a total score. A score higher than or equal to the cut-off point of 6 indicates the existence of a mild mental disorder. The sensitivity and specificity of SRQ-20 are 84.8% and 83.7%, respectively.<sup>(19)</sup>

### Data analysis

All data analyses were performed using STATA version 11. To analyze the association of social support and CMD, bivariate analysis was done by the chi-square test. To identify the factors associated with PE/E, bivariate matched

analysis was done by comparing the cases and controls (1 case: 1 control) for each variable of interest and crude matched odds ratio and their 95% confidence intervals along with p values were calculated using McNemar's test. In multivariate analysis, matched analysis in logistic regression was performed to identify associated factors of PE/E while adjusting for other variables. Finally any variable with p-value > 0.05, and not a confounder or interacting with other variables, were removed from the model to obtain a parsimonious and biologically meaningful model that best explains the phenomena of PE/E.

### Ethical Clearance

Written informed consent was obtained from all women, and the study was approved by the Ethical Review Board of Gadjah Mada University.

### RESULTS

The socio-demographic, obstetric and antenatal characteristics of all participants are presented in Table 1. The actual sample size achieved was a total of 143 cases matched on maternal age and parity with 143 controls participating in the study of preeclampsia risk factors. There were 103 nulliparous/primiparous women and 40 multiparous women with single pregnancy. No significant differences were observed between cases and controls with regard to family structure, social support, maternal age, inter-pregnancy interval, parity, history of abortion, pre-pregnancy BMI, history of ANC, and history of contraception used. A total of 45.10% of respondents had low social support, and 27.27% of respondents were positive for CMD (Table 1).

Table 2 shows that some of the variables significantly associated with the incidence of PE/E are: CMD (+) ( $p < 0.01$ , OR = 6.11, 95% CI: 2.99 to 14.07), low family income ( $p < 0.01$ ; OR = 2.93, 95% CI: 1.56 to 5.82), history of chronic hypertension (+) ( $p < 0.01$ , OR = 7.67, 95% CI :

2.32 to 39.89), and history of hereditary of PE/E (+) ( $p = 0.01$ , OR = 6. 95% CI: 10.34 to 55.20). Multivariate analysis was performed to obtain any factors associated with PE/E (Table 3).

The second model is better than the first model, as can be seen from the difference BIC1-BIC2 = -4,625, which means a positive support the second model. However, pseudo-R<sup>2</sup> = 0,3254, which means that the independent variable in the equation of the second model is able to explain the relationship between the PE/E incidence of 32,54% and while the remaining 67.46% is explained by the other variables

### DISCUSSION

Low family income per month is significantly associated with incidence of PE/E. Low socioeconomic status is a strong risk factor for incident PE.<sup>(20)</sup> Another study found that socioeconomic status is not associated with the occurrence PE.<sup>(5,21)</sup> Some researchers concluded that women with more advanced socioeconomic rarely infected with PE, whereas in epidemiological studies well controlled, found that the incidence of PE did not differ between socioeconomic classes.<sup>(3)</sup> In lower socioeconomic groups is likely to have lifestyle/behavior of a lack of exercise and poor nutritional intake. Lack of exercise has been associated with cardiovascular health, diabetes and others leading to poor of pregnancy outcomes.<sup>(22)</sup> Regular exercise can reduce the risk of hypertensive disorders in pregnancy.<sup>(23)</sup> Lower socioeconomic groups are also related to the daily nutrient intake, weight gain patterns during pregnancy and what to eat contribute to a poorer pregnancy outcomes.<sup>(24)</sup> In countries with low- and middle-income, pregnant women are at higher risk for experiencing CMD because of the increased burden of risk factors such as lack of economic, domestic violence, drug abuse and lack of support sosial.<sup>(10)</sup>

The results of this study showed no direct relationship with the incidence of social support PE/E. Psychosocial assets have a buffering

Table 1. Comparability between cases and controls by characteristics of respondents

Variables	Cases		Controls		p McNemar
	n	(%)	n	(%)	
Family income					
Low	75	52.45	48	33.57	0.001
High	68	47.55	95	66.43	
Family structure					
Extended family	63	44.06	60	41.96	0.771
Nuclear family	80	55.94	83	58.04	
Social support					
Low	71	49.65	66	46.15	0.597
High	72	50.35	77	53.85	
CMD*					
Yes	62	43.36	16	11.19	0.001
No	81	56.64	127	88.81	
Maternal age					
< 20 years old dan > 35 years old	44	30.77	44	30.77	1.000
20-35 years old	99	69.23	99	69.23	
Inter-pregnancy interval					
>4 years	63	44.06	55	38.46	0.230
<4 years	80	55.94	88	61.54	
Parity					
Nulliparous/primiparous	103	72.03	103	72.03	1.000
Multiparous	40	27.97	40	27.97	
History of abortion					
No	121	84.62	126	88.11	0.473
Yes	22	15.38	17	11.89	
History of chronic hypertension					
Yes	31	21.68	11	7.69	0.001
No	112	78.32	132	92.31	
History of PE/E <sup>®</sup>					
Yes	11	7.69	0	0	0.001
No	132	92.31	143	100.00	
Hereditary of PE/E					
Yes	12	8.39	2	1.40	0.013
No	131	91.61	141	98.60	
Pre-pregnancy BMI <sup>§</sup>					
> 25	25	17.48	21	14.69	0.636
< 25	118	82.25	122	85.31	
History of ANC <sup>#</sup>					
< 4 times	9	6.29	5	3.50	0.424
≥ 4 times	134	93.71	138	96.50	
History of contraception used					
Yes	46	32.17	49	34.27	0.755
No	97	67.83	94	65.73	

\*CMD=common mental disorders; <sup>®</sup> PE/E= pre-eclampsia/eclampsia; <sup>§</sup> BMI= body mass index; <sup>#</sup> ANC = ante natal care

effect on the events of life, pregnant women who report many change of life events during pregnancy, low psychosocial assets had a higher complication rate compared to women with high psychosocial assets. Psychosocial assets are measured in five dimensions: ego strength,

quality of marriage, relationships with family, social resources, including patterns of friendship and feelings about the pregnancy. However, mothers with many changes of life and low support had the highest complication rates. The assumption that the tangible support alone is not

Table 2. Relation between maternal socio-demographic characteristics and obstetrical history with PE/E

Variables	OR (95%CI) *	p
Family income	2.93 (1.56-5.82)	< 0.001
Family structure	1.14 (0.61-2.11)	0.771
Inter-pregnancy interval	1.62 (0.77-3.51)	0.230
History of abortion	0.72 (0.33-1.56)	0.473
History of chronic hypertension	7.67 (2.32-39.89)	<0.001
BMI <sup>®</sup> pra-pregnancy	1.22 (0.63-2.42)	0.636
History of ANC <sup>#</sup>	1.80 (0.54-6.84)	0.424
History of contraception used	0.86 (0.44-1.67)	0.755
History of PE/E <sup>§</sup>	**	**
Hereditary of PE/E	6.00 (1.34-55.20)	0.013
Social support	1.19 (0.69-2.09)	0.597
CMD <sup>¶</sup>	6.11 (2.99-14.05)	<0.001

\* Mc Nemar test; \*\* Cannot be calculated because all cells have zero values ; <sup>®</sup> BMI =body mass index; <sup>#</sup> ANC : ante natal care; <sup>§</sup> PE/E =pre-eclampsia-eclapsia; <sup>¶</sup>CMD= common mental disorders

a significant predictor because it is always combined with the emotional support for the prediction of pregnancy outcome, this is consistent with the buffering effect stress.

Another study found that systolic and diastolic blood pressure higher score was positively related to higher depressive symptoms, but did not correlate with the score of the support social.<sup>(25)</sup> While other studies have found that lack of social support lead to greater depressive

symptoms, has also been associated with high blood pressure among American Afrika.<sup>(26)</sup> Chronic hypertension is an independent risk factor for the incidence of PE/E, especially superimposed preeclampsia.<sup>(27-29)</sup> Hypertension can be caused by vasospasm or vasoconstriction. Vasospasm itself may cause damage to blood vessels. This change will cause endothelial damage and leakage in sub-endothelial cells that cause blood constituents, including platelets and

Table 3. Modeling of conditional logistic multiple regression between social support plus external variables and PE/E

Variables	First model			Second model		
	aOR*	95% CI	p	aOR	95% CI	p
CMD <sup>®</sup>	6.40	2.90-14.12	<0.001	6.52	2.96-14.37	<0.001
Family income	2.92	1.40-6.11	0.004	2.81	1.36-5.80	0.005
History of hypertension	5.76	1.36-24.45	0.018	6.06	1.45-25.36	0.014
Hereditary PE/E <sup>#</sup>	7.46	1.13-48.93	0.037	7.14	1.12-45.47	0.037
Inter-pregnancy interval	1.29	0.53-3.11	0.579			
Goodness of fit						
Pseudo-R <sup>2</sup>		0.3269			0.3254	
LR <sup>§</sup>		64.81			64.50	
p		<0.001			<0.001	
BIC <sup>¶</sup>		-39.995			-44.648	
BIC difference					-4.625	
n		286			286	

\*aOR=adjusted Odds Ratio by family income, history of hypertension, hereditary PE/E, and inter-pregnancy interval; <sup>®</sup> CMD=common mental disorders; <sup>#</sup> PE/E =pre-eclampsia/eclapsia; <sup>§</sup> LR= likelihood ratio; <sup>¶</sup> BIC=Bayesian information criterion

fibrinogen precipitate in subendotel.<sup>(3)</sup> Results of multivariable analysis showed that low social support increased the risk 1.38 times the incidence of PE/E after controlling for a history of chronic hypertension variable, although still not statistically significant. In this study it was found that the cases reported to have high social support. The case of pregnant women with PE, including high risk and will be monitored closely by a midwife during ANC services including more frequent ANC visits, home visits, monitoring by phone, measurement of blood pressure and asks for the development through changes in symptoms and examination of urine protein. In addition, there are habits of pregnant women, especially for a first pregnancy at 8 months of gestation aged, pregnant women will be reunited with their parents or their families for childbirth preparation. This is likely to contribute to the perception of high social support.

Although there is no direct relationship between social support with the incidence of PE/E, but there are differences in low social support in pregnant women with and without CMD (92.3% vs. 31.3%). Low social support increased the risk 26.4 times for the event CMD. The results of a prevalence study of the prevalence of other CMD increased in pregnant women who do not have relates in the community and lived in crowded household.<sup>(10)</sup> Crowded household as a chronic stressor adverse psychological well-being, contribute to psychological distress, unhappiness, irritability can even cause a person to think of suicide. Lack of privacy and the perceived demands in the crowded household, is also strongly and consistently associated with welfare. Families with psychosomatic complaints have redundant protection characteristics (overprotection), excessive involvement (over involvement) family members with one another and excessive pressure (overemphasis) in the role of social nurture support.<sup>(30)</sup> Social support have an influence on depressive symptoms in mothers pregnant.<sup>(31)</sup> To clarify why social support

affects physical and mental health conditions, more study is needed to determine how life events experienced by respondents and specify social support in the form of emotional support, instrumental support, the support judgment or support information as well as how the quality of relationships within the family. It is estimated that social support can affect physical and mental health through its influence on emotions, cognition and behavior. Good social support can act as a buffer against stress, thus preventing of diseases.<sup>(32)</sup> Combination of oxytocin and social support showed the lowest cortisol concentration and calmness and decreased anxiety during stress.<sup>(33)</sup>

The results obtained that CMD increases the risk six times more to the incidence of PE/E. The results of other studies found depression and anxiety in early pregnancy is associated with risk PE. Similarly, a history of anxiety and mood disorders in pregnant women increases the risk 2.13 times the incidence of PE after controlling for the variables age, race, and BMI before pregnant.<sup>(34)</sup>

The relationship between CMD with the incidence of PE/E can be proved biologically plausible. Conditions of distress (depression, anxiety and stress) during pregnancy leads to the incidence of PE with elevated levels of cortisol and changes in the sensitivity of lymphocytes to glukokortikoid. High levels of cortisol during stress conditions may also induce hypertension and dysfunction endotel.<sup>(6)</sup>

Several limitations must be considered when interpreting the results from our study. First of all recall bias and inability to establish temporality between preeclampsia and certain variables are inherent due to the matched case control study design. We cannot exclude the possibility that our results could be partially confounded by unidentified risk factors. Prepregnancy weights and body mass index (BMI) were assessed by subtracting the average weight gain from the full term maternal weight which might not be a good proxy measure as well as social support.

## CONCLUSIONS

Low social support is not directly associated to the incidence of PE/E. CMD is more common in pregnant women with PE/E. Future study is needed to clarify the influence of low social support on the incidence of PE/E by way of improved methodology, specify social support into the emotional support and instrumental support and the quality of relationships within the family.

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