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RESEARCH ARTICLE

Correlation between Endothelin-1 Levels and Mean Arterial Pressure (MAP) in Pregnant Women with Preeclampsia

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ABSTRACT

Introduction: **Preeclampsia is a common obstetric complication worldwide associated with maternal and perinatal morbidity and mortality. Hypertensive disorders of pregnancy (HDP) are characterized by high blood pressure and proteinuria after the 20th week of gestation which can result in eclampsia and multiple organ failure. The increased release of ET-1 in preeclampsia may have vascular constrictor effects and therefore the high concentration of ET-1 may be related to hypertension, because ET-1 is a potent vasoconstrictor. Estimation of association between ET-1 and mean arterial pressure (MAP) would aid in defining the predictions for further progress of the preeclamptic women into severe disease.**

Method: **This study is an analytic correlational study carried out at the Prof. Dr. I. G. N. G. Ngoerah Hospital, Denpasar, with subjects of pregnant women with preeclampsia who met the inclusion criteria. MAP was recorded and the serum samples were collected for ET-1 level measurement with the ELISA method. A consecutive sampling method was used to achieve a sample size of 50 participants.**

Results: **The study found a significant positive correlation between ET-1 levels and MAP in preeclamptic subjects, suggesting that ET-1 elevation is associated with increased MAP, further supporting the role of ET-1 in the pathophysiology of preeclampsia-related hypertension.**

Conclusion: **ET-1 levels correlate positively with MAP, indicating a potential diagnostic marker for preeclampsia progression.**

Keywords: Endothelin-1, hypertension, mean arterial pressure, preeclampsia.

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1. Introduction

Preeclampsia is one of the most severe and widespread pregnancy complications on the planet and one of the greatest threats to both mother and fetus health. Development of rises in blood pressure (≥140/90 mmHg) and proteinuria (≥300 mg/24 hours) post 20 weeks of pregnancy are signs of severe preeclampsia, which can take form of eclampsia accompanied with seizures and an increased risk of maternal death [1]. Preeclampsia is among the leading causes of adverse pregnancy outcomes globally, constituting a major contributor to maternal and perinatal mortality rates. Many previous studies have investigated the impact of preeclampsia worldwide, with some statistics from the World Health Organization (WHO) reporting that maternal mortality rates from preeclampsia range from 0.51% to 38.4%, depending on the location [2]. The incidence rates in Indonesia are reported to be between 3.4% to 8.5% that emphasize the need for effective diagnostic and preventive measures, especially in regions with high prevalence [3], [4].

Although the fundamental causes of preeclampsia are still poorly understood and numerous, it is increasingly clear that an interplay between vascular, immunological, and genetic factors contributes to the condition. Recent research suggests that preeclampsia actually begins in the placenta, where reduced perfusion initiates a cascade of oxidative and inflammatory processes affecting maternal cardiovascular health [5]. This placental dysfunction leads to the main mechanism driving the disease; endothelial

dysfunction manifested as increased vascular resistance that stresses the mother's kidney and liver [6]. The high correlation with disease and treatment characteristics of these inter-related vascular effects underscores the relevance of further investigation of vascular biomarkers that could elucidate disease mechanisms in the future and inform earlier detection of conditions with a high risk of nephropathy.

Endothelin-1 (ET-1), a potent vasoconstrictor generally linked to impaired vascular function associated with preeclampsia, has been recognized as a potential biomarker. Preeclampsia has been shown to increase the production of endothelin-1 (ET-1), a potent vasoconstrictor that is produced by endothelial cells in response to stressors including hypoxia, in women with preeclampsia compared to women with normotensive pregnancies [7], [8]. High levels of ET-1 are associated with the pathophysiology of preeclampsia, particularly increased vascular resistance and hypertension [9]. Animal studies have also implicated a direct role for ET-1 in mediating the development of preeclampsia by demonstrating that ET-1 alone can induce pregnancy-dependent hypertension [10]. Therefore, investigating ET-1 may help to understand the underlying mechanisms of hypertension in preeclampsia and provide a more targeted approach to diagnosis.

Mean Arterial Pressure (MAP) has gained recognition in clinical practice as a significant predictor of pregnancy-related hypertension diseases, especially preeclampsia. Pregnancy-related cardiovascular stress can be measured by MAP, which represents the average arterial pressure during a cardiac cycle and offers crucial information on the perfusion of the mother's and fetus's organs [11]. With a detection rate of up to 72%, studies have shown that MAP is a useful tool for predicting preeclampsia, especially when assessed in the second trimester [12]. Examining both measurements may provide a more complex and precise prediction model for preeclampsia risk and severity, given the correlation between elevated ET-1 levels and high MAP values in preeclamptic patients.

In view of these associations, the present study is designed to further explore the association of MAP with ET-1 levels in pregnant women with preeclampsia. This study aims to investigate ET-1 as a marker of hypertension and its association with MAP, and thereby to improve the diagnostic accuracy for preeclampsia and possibly detect the need for early intervention. Understanding of this association may be useful for the management of preeclampsia that will help the mother and the fetus in the future.

2. Materials and Methods

The study used an analytical correlational design to examine the relationship between Mean Arterial Pressure (MAP) and Endothelin-1 (ET-1) levels in pregnant patients with preeclampsia at the Obstetrics and Gynecology Department's Delivery Room at Prof. Dr. I.G.N.G. Ngoerah Hospital in Denpasar. Patients diagnosed with preeclampsia who were over 20 weeks of gestation were included in the study via successive sampling, which was carried out from January 2023 until the sample size was attained. ELISA was used to measure the ET-1 levels in serum samples, and blood pressure readings were used to record MAP. Patients have to meet standardized diagnostic criteria for preeclampsia and have a singleton pregnancy in order to be eligible. Statistical analyses were conducted with SPSS v25, allowing for a thorough evaluation of the relationship between ET-1 levels and MAP, and enhancing understanding of vascular changes in preeclamptic patients.

3. Results

Data from the Obstetrics and Gynecology Department's Delivery Room at Prof. Dr. I.G.N.G. Ngoerah Hospital Denpasar in 2023 were used in the study. Of the 50 preeclamptic participants, 47 (94%) had elevated Endothelin-1 (ET-1) levels above 5 pg/mL, while only 3 (6%) were within the normal range (0.7 to 5 pg/mL). With a mean of 16.48 pg/mL, ET-1 levels varied from 3.96 pg/mL to 58.57 pg/mL. Every participant had MAP values above 100 mmHg, with an average of 129.14 mmHg, a minimum of 112 mmHg, and a maximum of 145 mmHg. Additional information is displayed in Table I.

With a correlation coefficient of 0.711 and a p-value of 0.0001 ($p < 0.05$), statistical analysis employing Spearman's correlation revealed a robust and statistically significant link between ET-1 levels and MAP.

With an R^2 value of 0.346, the scatter plot in Fig. 1. indicated a linear trend between ET-1 and MAP, indicating that variations in ET-1 levels may account for about 34.6% of the variation in MAP.

4. Discussion

The demographic and clinical characteristics of pregnant women with preeclampsia were the main focus of this study, which also evaluated the sample population's mean arterial pressure (MAP), age, parity, and endothelin-1 (ET-1) levels. The bulk of participants (66%) were in the 20–35 age range, which is consistent with other research findings. Preeclampsia and eclampsia cases were more common in the same age group, according to Sumampouw et al. [12], especially in cases treated at RSUP Prof. Dr. R. D. Kandou Manado. Additionally, Pardede et al. [13] discovered a strong relationship between age and the occurrence of preeclampsia, with the age range of 21–35 years being the most impacted. This pattern confirms the notion that preeclampsia onset is more common in mothers who are younger. The timing of preeclampsia manifestation may be influenced by age-related physiological parameters, as Ukah et al. [14] found that older maternal age was associated with late-onset instances but did not significantly change the risk of severe preeclampsia.

TABLE I: Sample Characteristics

Parameter	Minimum	Maximum	Mean
Age	14	42	30.82
Parity	0	4	1.12
ET-1 (pg/mL)	3.96	58.57	16.4778
MAP (mmHg)	112	145	129.14

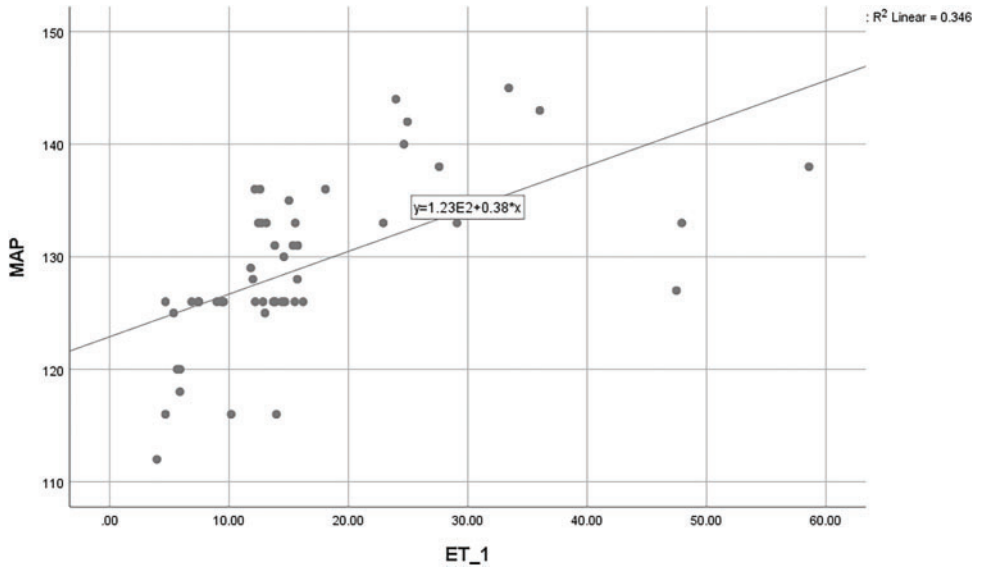

Fig. 1. Scatterplot showing ET-1 with MAP.

In this study, parity analysis showed that 38% of participants were nulliparous, 4% had more than three prior births, and 58% had given birth one to three times. Different levels of risk have been linked to parity in previous research; for example, Nur et al. [15] discovered that primigravida women had a 5.59-fold increased risk of preeclampsia. Opitasari et al. [16] also confirmed that women who are nulliparous have a markedly increased risk of developing severe preeclampsia in comparison to those who are multiparous. In contrast, Tyas et al. [17] found that multiparous women had higher rates of severe preeclampsia (81.4%, $p < 0.001$), suggesting that parity risk may differ among populations as a result of genetic, environmental, or medical variables.

With 94% of the sample having ET-1 levels over 5 pg/mL and a mean level of 16.48 pg/mL, this study's noteworthy finding was the high ET-1 levels in preeclamptic women. Research on preeclampsia has extensively reported elevated ET-1; for example, Hartati et al. [18] demonstrated that preeclamptic patients typically have greater ET-1 levels than pregnant women with normotension. According to Adusu [19], ET-1 is a useful biomarker for differentiating between cases of moderate and severe preeclampsia. This suggests that cases with severe clinical signs may be more likely to have elevated ET-1. The idea that ET-1 may contribute to vascular smooth muscle contraction and elevated blood pressure, two characteristics of preeclampsia pathophysiology, was supported by similar findings published by Hasnah et al. [20], who found markedly elevated ET-1 expression in the umbilical vessels of preeclamptic women.

With an average MAP of 129.14 mmHg, every participant in this study had elevated MAP readings. This outcome is in line with research by Mayrink et al. [21], who discovered that MAP is a good prognostic marker for preeclampsia, particularly when the condition manifests early. Their research showed that early-onset preeclampsia was substantially correlated with elevated MAP at 20 weeks gestation, whereas late-onset patients had elevated MAP at 37 weeks. This demonstrates how MAP monitoring at key gestational stages may be useful for the early detection and treatment of preeclampsia. The predictive accuracy of MAP for preeclampsia in Asian populations was further validated by Zhu et al. [22], who found that it performed better than uterine artery Doppler measures and angiogenic factors, highlighting MAP's worth as a dependable, long-term monitoring technique.

This study's considerable correlation between MAP and ET-1 levels ($p < 0.0001$; $r = 0.711$) demonstrates the robust, positive relationship between these parameters, with fluctuations in ET-1 accounting for approximately 34.6% of MAP variability. A similar linear relationship between ET-1 and blood pressure components was previously shown by Salindeho [23], indicating that elevated ET-1 levels cause increases in both systolic and diastolic blood pressures, which in turn affect MAP. Additionally, Shaarawy and Abdel-Magid [24] confirmed that in preeclamptic women, ET-1 release increases MAP and worsens the severity of the condition. These results advance our knowledge of the potential pathways by which ET-1 mediates systemic vascular resistance and endothelial dysfunction in preeclampsia, resulting in widespread hypertension and related consequences.

The study's findings collectively support the important roles that maternal age, parity, ET-1, and MAP play as risk factors and indicators in the clinical treatment of preeclampsia. Particularly, elevated MAP and ET-1 levels offer valuable information on the pathophysiological mechanisms of preeclampsia, bolstering the idea that these indicators could be used as therapeutic targets and predictors in the management of high-risk pregnancies. To enhance therapeutic outcomes for preeclamptic patients and improve predictive models, more study is advised to examine the longitudinal effects of these factors across a range of populations.

5. Conclusion

With a correlation coefficient of 0.711, which explains 34.6% of the variability in MAP, this study demonstrates a statistically significant positive association between endothelin-1 (ET-1) levels and MAP in pregnancies complicated by preeclampsia. According to these findings, ET-1 may play a role in the pathophysiology of high MAP, making it a promising biomarker for determining the severity of preeclampsia. Clinicians may increase the early detection of preeclampsia and better focused therapies by integrating ET-1 level monitoring into early screening and risk assessment. This strategy may thereby enhance maternal and fetal outcomes while lowering morbidity associated with preeclampsia. To validate ET-1's usefulness as a biomarker across a range of patient populations, more investigation should be done into its function in larger clinical contexts.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

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