

Analysis of Endothelin-1 (ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women

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Received June 30, 2024; Revised September 23, 2024; Accepted October 12, 2024

Cite This Paper in the Following Citation Styles

(a): [1] Nur Inayah Adam, Andi Ariyandy, Irfan Idris, Werna Nontji, Sri Ramadhany, Stang, "Analysis of Endothelin-1 (ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women," *Universal Journal of Public Health*, Vol. 12, No. 6, pp. 1122 - 1130, 2024. DOI: 10.13189/ujph.2024.120609.

(b): Nur Inayah Adam, Andi Ariyandy, Irfan Idris, Werna Nontji, Sri Ramadhany, Stang (2024). *Analysis of Endothelin-1 (ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women*. *Universal Journal of Public Health*, 12(6), 1122 - 1130. DOI: 10.13189/ujph.2024.120609.

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Abstract Due to the rising incidence of obesity, notably in Indonesia, it has become a major worldwide health concern. Obesity in pregnant women can cause various health complications for the mother and fetus. One powerful vasoconstrictor peptide that is implicated in many physiological and pathological processes, including endothelial damage, is endothelin-1 (ET-1). The purpose of this study is to compare the levels of ET-1 in the urine of obese and non-obese pregnant women. The present cross-sectional research was carried out in Gorontalo City and included a sample of pregnant women aged 25-30 who were overweight or obese, second-time mothers, third-time mothers, and in their second trimester of gestation, in addition to pre-pregnancy obese and GWG obese pregnant women. These females weren't overweight. The research sample included 75 individuals in total, and the Consecutive Sampling technique was used to divide them into three groups. The ELISA method was used to find ET-1 levels, and the sample was created using information from interviews and physical examinations. The data analysis used the Independent Sample T-tool statistical method to compare groups consisting of non-obese pregnant women, pre-pregnancy obese pregnant women, and GWG obese pregnant women. According to the results, pre-pregnancy obese pregnant women had greater ET-1

levels in their urine (137.85 ng/l) than non-obese pregnant women (109.39 ng/l) or GWG obese pregnant women (107.21 ng/l). Pregnant obese women who have high levels of ET-1 in their urine may be at risk for kidney injury.

Keywords Endothelin-1 Urine, Obesity, Pregnancy, Kidney Damage

1. Introduction

Obesity has now become a very significant health issue, considering the increasing prevalence that occurs almost throughout the world, making Obesity an ongoing epidemic [1]. The number of people with overweight and obesity issues has been increasing rapidly worldwide [2]. Overweight gain results in obesity, which is recognized as the primary cause of many illnesses, such as Type II Diabetes, heart disease, hypertension, hyperlipidemia, and several malignancies. The high risk of early mortality is thought to be mostly caused by obesity [3]. Global obesity prevalence is more than quadrupled between 1990 and 2022. The World Health Organization projects that by 2022, over 2.5 billion people globally would be overweight or

obese, with over 890 million of them being obese. According to WHO estimates, 43% of individuals who are 18 years of age or older are overweight, with 44% of women and 43% of men being overweight. This is concerning since, by 2019, obesity-related disorders will claim the lives of at least 5 million people annually [4].

These National Medium Term Development Plan (RPJMN) indicators cover the years 2015–2019, the proportion of overweight adults in Indonesia, at 13.5%, is higher than that of obese adults ($BMI \geq 25$) and obese adults ($BMI \geq 27$), at 28.7% [5]. Information from the Indonesian Health Survey (IHS) for 2023 indicates that the percentage of obese individuals has risen from 21.8% in Riskesdas 2018 to 23.4%. Obesity prevalence in people over the age of 18 is 14.4% ($BMI \geq 25$) and 23.4% ($BMI \geq 27$), according to the Indonesia Health Survey (IHS) 2023 [6].

It has been observed that women have higher incidence or prevalence rates of obesity than males do, with women of reproductive age having seen a notable rise in obesity over the last three decades [7,8]. Over 25 percent of women worldwide are predicted to be obese by 2025. Pregnancy-related obesity presents a major challenge to obstetric care due to its prevalence and potential harm to the fetus and mother. From 2010 to 2019, the estimated prevalence of maternal obesity pregnancies globally was 16.3%, or one in six pregnancies [9]. Between 2017 and 2018, the percentage of Americans who were obese fell to 40% [10]. During 9–10% in the first half of the 1990s to 16–19% in the 2000s, the UK saw a rise in the proportion of obese pregnant women. An estimated 11% of Indian Subcontinent residents were married to obese or overweight women between the ages of 15 and 49. This number rose to 15% in the fourth National Family Health Survey (2006–2007) and 20.6% in the 46th [11].

In 2014, it was estimated that 326,900 pregnant individuals were obese in Indonesia [11], and according to study by Sudhityasa [12] in [13], in the population of pregnant women, there were 25% obese individuals. With 32% of Indonesia's overall population in this age bracket, the number is much greater [13]. Conversely, in the Gorontalo City region, the percentage of pregnant women who are obese may approach 35% of all pregnant women in their various work locations, according to preliminary research using midwife interviews in several Gorontalo City Health Service operational regions. A projection from the Gorontalo City Health Service states that in 2022, 35 pregnant women are expected to be distributed throughout 10 Health Center (Puskesmas) labor zones. There will be 2439 pregnant women globally in August 2023, according to data [14]. Overweight gained during pregnancy and pre-pregnancy obesity are examples of maternal obesity, or obesity that develops throughout pregnancy (GWG) [15]. Obesity raises the likelihood of pregnancy complications and health concerns for both the mother and the baby, as is often known [16]. According to research by [17] and [8], women who are overweight or obese during pregnancy are more likely to have challenges connected to their

pregnancy and to give birth to a child who has negative outcomes, such as autism spectrum disorders (ASD). Also, there is a greater chance that children of fat moms would grow up to experience obesity, cardiovascular illness, and neuropsychiatric issues, among other chronic conditions [1,8].

Additional studies indicate that obesity is a common obstetric issue that affects mothers' short- and long-term health. These issues include an increased risk of postpartum hemorrhage, venous thromboembolism, gestational diabetes, hypertension, caesarean section delivery, and maternal death. Additionally, obese women are more likely to acquire excessive weight during pregnancy [18].

2. Materials and Methods

2.1. Research Design

This study used a cross-sectional design to compare and assess the levels of endothelin-1 (ET-1) in the urine of pregnant women who weren't obese versus those who were. Pregnant women classified into three categories were included in the research population: non-obesity pregnant women, pre-pregnancy obese pregnant women, and gestational weight increased pregnant women. The samples for this study were obtained through consecutive non-probability sampling. The pregnant women were registered in the Gorontalo City Health Service workforce (GWG).

2.2. Research Setting and Participants

After the research permit was issued, the research was conducted at eight health centers (Puskesmas) in the working area of the Gorontalo City Health Office from February 2024 - April 2024. Samples of pregnant women were taken according to the criteria during the Ante Natal Care (ANC) examination at each health center, including a sample of pregnant women aged 25-30 who were overweight or obese, second-time mothers, third-time mothers, and in their second trimester of gestation, in addition to pre-pregnancy obese and GWG obese pregnant women. 75 pregnant women in total, split into three sample groups of 25 pregnant women each, made up the samples that were collected. The levels of endothelin-1 (ET-1) in the urine of pregnant women who were obese and those who were not were measured and compared using a cross-sectional methodology in this research. However, numerous pregnancies, heart disease, dyslipidemia, gestational diabetes, and other chronic conditions are grounds for exclusion for expectant mothers.

2.3. Research Instrument

Data was collected through structured interviews and physical examinations to obtain demographic and clinical data. At the same time, urine samples were taken and stored

at freezer -32 °C to analyze ET-1 levels using the Enzyme-Linked Immunosorbent Assay (ELISA) technique in the clinical laboratory with standard procedures to ensure the accuracy and reliability of the results.

2.4. Research Procedure

The research begins by registering pregnant women at the local health center (puskesmas). Participation as a responder is open to women who fit the inclusion requirements. By requesting respondents to fill out a permission form, the researcher acquired their agreement. She identified herself as a midwife and student in Hasanuddin University's master of midwifery studies program.

Before the intervention began, the necessary research instruments and materials were prepared, including cool boxes containing ice gel, urine pots, and urine protein test sticks, as well as standard operating procedures (SOP) for urine sampling, where the researcher carried out the sampling. Each of the 75 respondents was questioned using a questionnaire sheet and had an anthropometric assessment. The respondents were split evenly into three groups: 25 non-obesity pregnant women, 25 obese pregnant women, and 25 obese pregnant women. Next, using a pee pot, the respondents took a sample of urine, which they then placed in a cold box at -5 °C for five to six hours. Finally, they placed the urine sample in a freezer, where it was kept between -29 °C and -32 °C. Finally, using a cool box to maintain a low temperature of around -5 °C, all collected samples were flown to the Hasanuddin University Medical Research Centre Laboratory in Makassar, South Sulawesi. The samples were stored at -80 °C in a freezer until they were analyzed in the lab using the Endothelin-1 ELISA Kit. According to the ELISA protocol, which describes the following, researchers examined the samples with the assistance of laboratory analyst officers. 1. Assemble all necessary materials, including reagents, standards, and samples. 2. Fill each well with samples and ELISA reagent. 3. Add substrate solutions A and B. 4. Wash the plate five times. 5. Let it incubate for one hour at 37 °C. 6. Add the stop solution and watch as the color develops; 7. After 10 minutes of incubation at 37 °C, read the OD value. In order to facilitate analysis, the test's outcomes were meticulously recorded on an observation sheet.

2.5. Data Analysis

The ET-1 levels of non-obese, pre-pregnancy, and Gestational Weight Gain (GWG) obese groups were compared using a Kruskal Wallis analysis, while the ET-1 levels of obese and non-obese pregnant women were compared using an unpaired t-test. Finally, Chi-Square was used to determine the homogeneity of respondents based on the data collected through interviews and anthropometry in the form of respondent characteristics. The statistical program SPSS, version 26, was used for all analyses, with

a significance threshold of $p < 0.05$. For the purpose of comparing two unpaired groups, a Mann-Whitney test was used in this investigation.

3. Result

Aims of this research are to compare the urinary levels of endothelin-1 (ET-1) in non-obese pregnant women, pre-pregnancy obese women, and gestational weight gain (GWG) obese women.

Pregnancy-related obesity, pre-pregnancy obesity, and obesity with gestational weight gain (GWG) were the three groups of pregnant women examined in this study for their levels of endothelin-1 (ET-1). Eight health facilities in the Gorontalo City operating area were used for the sampling of pregnant women who attended Ante Natal Care (ANC). 75 respondents made up the overall sample size, which was split into three groups: 25 pregnant women who were not fat, 25 pregnant women who were obese before becoming pregnant, and 25 pregnant women who were obese GWG.

The data presented in Table 1 highlights the consistent frequency distribution of characteristics of pregnant women respondents based on three groups: non-obesity, pre-pregnancy obesity, and GWG obesity. Every responder was between the ages of 25 and 30. Pregnant GWG women who were either obese or not obese fell into the normal category, whereas the pre-pregnant obese women group fell into the obese category. This is based on the BMI distribution of respondents before pregnancy. Conversely, with respect to the present BMI, the pre-pregnant obese pregnant women group and the GWG obese pregnant women group both had 100% of their members in the normal category and 100% in the obese category. Pregnant women have normal LILA, with 100% of them having LILA greater than 23.5 cm. Every responder, with a gestational age ranging from 13 to 27 weeks, is in the second trimester of pregnancy. Out of the three respondents' groups, the majority did not meet the highest frequency in the area of weight growth. Of these, 22 individuals (88%), were classified as obese pregnant women. In the Urine Protein analysis, most respondents across the three groups exhibited (-) 0 mg/dl findings, with the highest prevalence in the GWG obese pregnant women group, comprising 24 individuals (96%). There is a variation in the number of respondents regarding the presence or absence of obesity in the family among the three groups of respondents. Among the group of respondents consisting of pre-pregnant obese women with a history of obesity in the family, the largest number is 17 people (68%), while the group of respondents consisting of non-obese pregnant women has as many as 16 people (64%). A p-value larger than the significance level of 0.05 indicates that there is no difference in the characteristics of respondents or respondents in all homogenous groups, according to the results of the chi-square test of all respondent characteristics.

Table 1. Characteristics of Respondents from Non-Obese Pregnant Women and Obese Pregnant Women

Parameter	Non-Obesity (n=25)	Obesity Pre-Pregnancy (n=25)	GWG Obesity (n=25)	p-value
^a Age (year)	27.52±1.61	28.48±1.69	26.72±1.81	0.466
^a Body mass index(kg/m2)				
Pre-Pregnancy	21.12±1.81	28.51±3.24	22.95±1.73	0.270
Now	22.34±1.94	31.65±4.01	27.37±1.62	0.264
^a Second trimester of pregnancy (weeks)	21.88±4.26	22.08±4.52	24.20±4.07	0.382
^b Weight Gain				
In accordance	10(40)	6(24)	3(22)	0.289
It is not in accordance with	15(60)	19(76)	22(88)	
^b Urine Protein (mg/dl)				
(-) 0	22(38)	21(84)	24(96)	0.439
(-) 10	3(12)	3(12)	1(4)	
(+) 30	0(0)	1(4)	0(0)	
^a Systolic Blood Pressure	108.80±12.69	118±9.13	111.20±10.92	0.418
^a Diastolic Blood Pressure	70.80±7.02	75.20±9.18	72.80±9.8	0.424
^b Family History of Obesity				
There is	9(36)	17(68)	11(44)	0.446
There isn't any	16(64)	8(32)	14(56)	

n = number of samples

a=numerical variable parameter (mean ± standard deviation)

b=categorical variable parameters

p-value = analysis of homogeneous characteristics of respondents, Chi-Square

3.1. Frequency Distribution of Urinary Endothelin-1 (ET-1) Levels, in Each Group

The information shown in Table 2 indicates that the average urine ET-1 level of the respondents was 121.00 ng/l, with a minimum and a maximum of 50.94 and 295.59 ng/l, respectively. Because of the non-normal distribution of the data, the mean value that was determined also included the median, minimum, and maximum values. Figure 1's graph displays the distribution.

Table 2. Frequency Distribution of Endothelin-1 (ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women

Endothelin-1 Levels	Non-Obesity	Pre-pregnancy	GWG Obesity
Mean	115.06	146.85	124.84
Median	109.39	137.85	107.21
SD	47.11	42.78	69.74
Minimum	50.94	94.88	52.40
Maximum	254.44	255.04	295.6

SD= Standard Deviation

Test: Descriptive

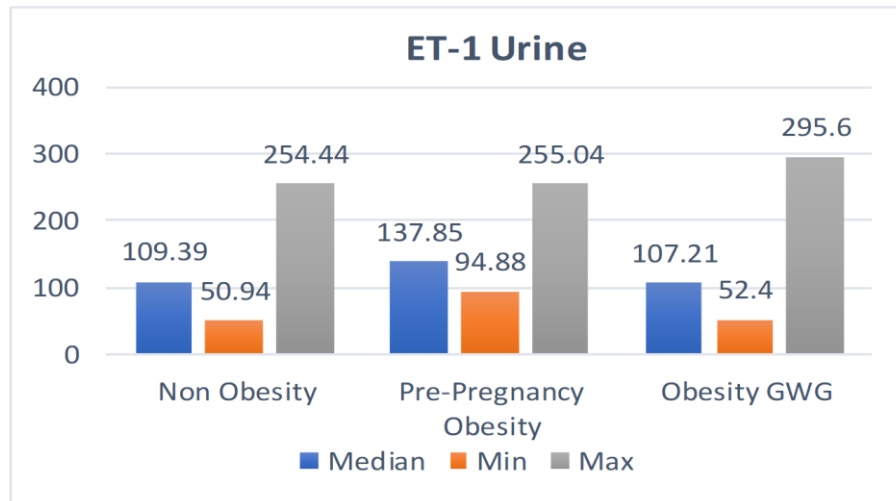


Figure 1. Urinary Endothelin-1 levels between groups of pregnant women

3.2. Comparison of Urinary Endothelin-1 (ET-1) Levels in Non-Obese Pregnant Women and Obese Pregnant Women

Based on the information in Table 3’s Kruskal–Wallis test results, it can be deduced that there is a noteworthy distinction in urine levels of Endothelin-1 (ET-1) between non-obese pregnant women, pre-pregnant obese women, and obese women based on weight gain during pregnancy (GWG). The group of pre-pregnant obese women had the highest Mean Rank result (48.40 ng/l) compared to the groups of pregnant women with GWG obesity (32.92 ng/l) and the non-obese pregnant women (32.68 ng/l). The significance value, or p-value, of 0.014 ($p < 0.05$), indicates a significant difference in the mean value of urinary endothelin-1 (ET-1) levels between the non-obese pregnant women, pre-pregnant obese women, and GWG (obese pregnant women).

Table 3. Comparison of Endothelin-1(ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women

Ranks		P-Value	
Group	n	Mean Rank	
ET – 1 Level	Non-Obesity	25	32.68
	Pre-Pregnancy Obesity	25	47.38
	GWG Obesity	25	32.92
Total		75	

Test: Kruskal Wallis

3.3. Comparison of the Effectiveness of Endothelin-1 (ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women

Further research was conducted using Post Hoc analysis since there was a substantial variation across the three

respondent groups. Since the data in this instance are not regularly distributed, the Mann-Whitney U test is used in the study. The purpose of this research is to identify differences between the two responder groups.

The information shown in Table 4 demonstrates studies were conducted to compare the prevalence of obesity among pregnant women with and without GWG ($p=0.009$), 0.977 and 0.015 among non-obese pregnant women and GWG pregnant women, and 0.977 and 0.015 among pre-pregnant obese pregnant women.

Table 4. Comparison of the Effectiveness of Endothelin-1(ET-1) Levels in the Urine of Non-Obese Pregnant Women and Obese Pregnant Women

Intervention	N	Mean Rank	Asym.sig (2 tailed)
Non-Obesity with Pre-pregnancy Obesity	50	20.12 ± 30.88	0.009
Non-Obesity with GWG Obesity	50	25.56 ± 25.44	0.977
Pre-Pregnancy with GWG Obesity	50	30.52 ± 20.48	0.015

Test: Post hoc, Mann-Whitney U

4. Discussion

This research uses a cross-sectional design to analyze and compare endothelin-1 (ET-1) levels in the urine of non-obese pregnant women, pre-pregnancy obese pregnant women, and GWG obese pregnant women. Three groups of pregnant women were included in the study population: non-obese pregnant women, pre-pregnancy obese pregnant women, and GWG (gestational weight gain) obese pregnant women. Samples were collected using consecutive non-probability sampling. The study population consisted of pregnant women working in the Gorontalo City Health Service. According to the results of this research, the group of respondents who were obese

before becoming pregnant as well as after being pregnant had a greater increase in weight gain throughout their pregnancies (GWG). Of the ten respondents (40%) in the non-obese group, six respondents (24%) in the pre-pregnancy obesity group, and three respondents (12%) in the GWG obesity group had appropriate weight gain. In contrast, 15 respondents (60%) in the non-obese group, 19 respondents (76%) in the pre-pregnancy obesity group, and 22 respondents (88%) in the GWG obesity group had inappropriate weight gain. Obesity-related pregnancy weight increase is common among expectant mothers [19].

The characteristics of the respondents' urine protein examination showed that most of the results were negative. However, one respondent (4%) in the pre-pregnancy obesity group had a dip protein level of + (30 mg/dl). There is an increase in urine protein during the third trimester of pregnancy [20].

In addition, a family history of Obesity was found in 68% of pre-pregnancy obese respondents, indicating that Obesity is also strongly influenced by genetic factors. Genes that direct signals to the immunological, endocrine, and neurological systems govern the ageing process of the kidneys [21].

A decrease in renal function is a sign of ageing, which is shown by elevated endothelin-1 (ET-1) concentrations in the kidneys. Moreover, an increased body weight is associated with age, especially in pregnancy. Weight gains during pregnancy are correlated with a mother's age. BMI before pregnancy can indicate the risk of Obesity, which affects kidney function through glomerular filtration [22]. The glomerular filtration rate and BMI of overweight pupils, according to previous research, are unrelated [23]. In the second trimester of pregnancy (13-27 weeks), pregnant women are generally in the healthiest period, with stable physiological and psychological adjustments. Physiological changes include increases in respiratory rate, blood volume, and glomerular filtration. Renal plasma increases by 85% during the second trimester due to increased cardiac output and vasodilation. Women who are pregnant but have not yet given birth have the highest systolic and diastolic blood pressure. Weight gain increases the risk of pregnancy-related problems including hypertension and pre-eclampsia [24].

From the analysis of Endothelin-1 (ET-1) levels in the urine of the group of pregnant women listed in Table 2, based on weight growth during pregnancy, it is evident that pregnant women with obesity issues before conception often have greater ET-1 levels than non-obese pregnant women and obese pregnant women. (GWG). Because there is no widely accepted standard value for endothelin-1 levels, neither in the literature nor in the system, the standard value of urine endothelin-1 is determined by measuring the levels of the hormone in normal pregnant women, who in this research are not obese. The mean ET-1 level in the pre-pregnancy obesity group was 146.85, higher than the non-obese group (115.06) and the GWG obesity group (124.84); this suggests that pre-pregnancy

obesity has a more significant impact on increasing ET-1 levels. The higher median (137.85) indicates that the midpoint of the distribution of ET-1 levels in the pre-pregnancy obesity group was more prominent, meaning that more than half of the respondents had high ET-1 levels. Depending on pre-pregnancy obesity indicates that pre-pregnancy obesity may influence the overall elevation of ET-1 levels in the population.

The more significant standard deviation in the GWG obesity group (69.74) indicates more variations in ET-1 levels in this group compared to the other two groups. This more significant variation may be due to the various factors influencing weight gain during pregnancy, such as diet, physical activity, and genetic factors. As in [25], pregnancy-related energy needs an increase by about 200, 300, and 400 kcal/day in the second and third trimesters, respectively. Nonetheless, research combining basal metabolic rate with water and individual physical activity using a total energy expenditure calorimeter has shown that these needs differ depending on body mass index (BMI). The minor standard deviation in the pre-pregnant obesity group (42.78) indicates that ET-1 levels were more consistent, indicating a more uniform effect of obesity before pregnancy. The minimum and maximum values in the table show the range of distribution of ET-1 levels within each group. The GWG obesity group had the highest maximum value (295.6), indicating the presence of some individuals with very high ET-1 levels.

The maximum value in the pre-pregnant obesity group was also high (255.04), while the non-obese group had the lowest maximum value (254.44). This range of values suggests that while pre-pregnancy obesity has a high mean and median, there is also a significant variation in ET-1 levels in the GWG obesity group.

Because obesity causes adipose tissue to produce proinflammatory adipokines and free fatty acids, it increases endothelial dysfunction and initiates the production of endothelin-1 [26]. Because adipocytes synthesize endothelial vascular cells found in the kidney. Adipose from obese mother releases ET-1 2-3 times in tissue and plasma more than normal mothers [27]. Restrictions on renal vascular resistance and the renal tubules' ability to transport water and ions depend on vascular endothelial cells [28]. Renal apoptosis and damage caused by ET-1 may be triggered by the induction of endoplasmic reticulum (ER) stress. The build-up of unfolded proteins in the ER is known as ER stress, and it induces cellular stress. In order to restore cellular equilibrium, cells react by initiating an adaptive open protein response that multiplies protein accumulation by further inhibiting protein transcription and translation and upregulating the expression of ER chaperones. But in the end, significant or protracted overexpression of these pathways results in organ damage and cellular death. For acute or chronic kidney illness, there is a wealth of data supporting the pathophysiologic function of ET stress [29].

Furthermore, endothelin is a potent renal vasoconstrictor,

significantly decreasing the glomerular filtration rate (GFR). Endothelin conveys its effects through at least two different receptor subtypes, namely ET-A and ET-B receptors; activation of each subtype can potentially decrease GFR [30]. The first half of a typical pregnancy should see an increase in both renal plasma flow (RPF) and glomerular filtration rate (GFR) of 40–65% and 50–85% over non-pregnant values, respectively. Based on micro puncture investigations, this augmentation is due to lower afferent and efferent arteriolar resistance without glomerular pressure alterations. The second week of pregnancy has resulted in a 25% rise in creatinine clearance [31]. So, this study shows that obesity and renal endothelin-1 have a positive correlation. This is in line with research [32]. It examined endothelin-1 levels in urine in obese adolescents and came to the conclusion that endothelin-1 in urine levels were greater in obese adolescents than in non-obese adolescents, allowing early kidney injury. ET-1 levels and insulin resistance in humans are also strongly correlated. Adipose tissue is also showing more and more evidence of the effects of ET-1, which vary based on the receptor-activated. Adipocyte-level ET-1 activation often increases glucose, glycerol, and plasma-free fatty acids while also promoting lipolytic activities and insulin resistance via a variety of routes [33].

Aside from that, vascular tone may be activated again by fat surrounding blood arteries. When there is visceral obesity, ET-1 contributes to elevated blood pressure. ET-1 is essential for controlling blood pressure, according to the findings. Endothelial dysfunction is hypothesized to be caused by an increase in ET-1 production in hypertensive individuals with increasing body mass. When endothelial ETA receptors are blocked, patients who are overweight or obese have considerable vasodilation; however, people with normal weight who are hypertensive do not [34]. Pregnant fat women have a greater systolic blood pressure than other categories of pregnant women, as may be seen.

Further evidence that pre-eclampsia is associated with a greater risk factor comes from the urine protein levels of pre-pregnant obese women who already have a positive urine protein one (+). Proteinuria and blood pressure increase in PE are independently determined by ET-1, which also functions as a renin suppressor. The study [35] showed a dose-dependent rise in ET-1 in mice given the VEGF inhibitor sunitinib, indicating that elevated ET-1 is a direct result of VEGF inactivation or suppression. They also reported a high association between sFlt-1 and plasma ET-1. There appears to be a vicious cycle of continuously rising circulating ET-1 in PE, which further impacts blood pressure, renal function, and renin-angiotensin system activity. This is because ET-1 itself causes oxidative stress in the placenta, which may lead to increased production of placental factors like sFlt-1.

Based on [36] in a study entitled *The Effect of Calcium Administration on Changes in Blood Pressure and ET-1 Levels in Pregnant Women with Pre-eclampsia*, the condition of obesity before pregnancy significantly impacts

endothelin-1 levels. Further research is needed to understand the mechanisms behind these elevated ET-1 levels and to explore interventions that can help manage ET-1 levels in obese pregnant women, both before and during pregnancy. Such interventions could include weight management programs, dietary changes such as a low-carbohydrate diet, high animal and vegetable protein, a diet low in fat, sodium, and sodium, as well as meeting the drinking water needs of 2-3 liters per day, and increased physical activity to maintain maternal and fetal health during pregnancy.

Pregnancy obesity, obesity based on weight increase during pregnancy, and non-obese pregnant women all had significantly different urine endothelin-1 (ET-1) levels, according to the findings of the Kruskal-Wallis test, which are shown in Table 3. There is a significant difference at the 5% significance level, as shown by the p-value of 0.014. So, both before and during pregnancy, obesity affects a woman's urine ET-1 levels.

With a mean score of 48.40, the pre-pregnancy obesity group outperformed the non-obese and GWG obesity groups, with mean ranks of 32.68 and 32.92, respectively. It demonstrates that obese women who were not previously pregnant often had higher urine levels of ET-1. Pre-existing obesity-related metabolic and inflammatory variables may be the cause of these diseases. Since pre-pregnancy obesity has existed longer than obesity brought on by excess weight gain (GWG) during pregnancy, it may also be connected to the length of obesity.

The comparison of ET-1 levels between two groups of respondents—non-obese pregnant women and pre-pregnant obese pregnant women ($p=0.009$) and between pre-pregnant obese pregnant women and GWG obese pregnant women ($p=0.015$)—revealed significant differences. This information was based on Table 4. Conversely, no difference was seen between pregnant GWG women who were obese and those who were not ($p=0.977$). The significant difference in ET-1 levels between groups may also indicate that weight gain during pregnancy (GWG) does not have as significant an impact as pre-pregnancy obesity on ET-1 levels. Although the GWG obesity group showed elevated ET-1 levels, their mean ratings were not as high as the pre-pregnancy obesity group. Although the GWG obesity group showed an increase in ET-1 levels, their mean rating was not as high as the pre-pregnancy obesity group, indicating that factors related to pre-pregnancy obesity were more dominant in influencing ET-1 levels compared to obesity due to weight gain during pregnancy itself [37]. This research is not in line with [26], which states that there is no significant difference in ET-1 levels in non-obese pregnant Wistar rats and non-obese pregnant Wistar rats. However, research [38] asserts that the differences between the fat and non-obese Wistar rats are noteworthy. The current study compared with a study that used rats as samples to measure Endothelin-1 levels in the body because research measuring Endothelin-1 levels in urine is new, and few

sources can make comparisons.

5. Conclusions

The significance of these findings lies in the correlation between elevated levels of ET-1 and a number of pregnancy-related problems, including preeclampsia and chronic kidney disease (CKD), which ultimately culminates in kidney failure. Consequently, controlling and monitoring ET-1 levels in obese expectant mothers particularly those who were fat before conception can be a crucial first step towards enhancing the health of both the mother and the fetus. Appropriate interventions, such as weight management programs in adolescents and women of childbearing age before conception and lifestyle changes through health education and intervention efforts, can help reduce ET-1 levels and the risk of associated complications. Pregnancy outcomes are thus improved, as is the long-term health of mothers and their offspring.

Acknowledgements

The author wants to extend her profound appreciation to all individuals who have made valuable contributions to this essay. Support, direction, and collaboration were crucial in completing this research. The author expresses her gratitude for the assistance and motivation that have offered.

REFERENCES

- [1] Andersen, C. S., et al, "Maternal Body Mass Index before Pregnancy as a Risk for ADHD and Autism in Children," *Eur Child Adolescence Psychiatry*, vol. 2, pp. 139-148, 2018. <https://doi.org/10.1007/s00787-017-1027-6>
- [2] Kukurova, Klaudia, et al., "The Problem of Overweight and Obesity - Does Geographical Location Matter?", *Universal Journal of Public Health*, vol. 9, no. 5, pp. 208-217, 2021. <https://doi.org/10.13189/ujph.2021.090502>
- [3] Banjarnahor, D., et al., "Risk factors of overweight and obesity in childhood and adolescence: A literature review," *Tropical Public Health Journal Faculty of Public Health, USU*, pp. 35-45, 2021.
- [4] WHO., *Obesity and Overweight, 2022* (Cited 2024 August 22)<https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>
- [5] Kemenkes. *National Health Report. Ministry of Health, Indonesia, 2022.*
- [6] Center for Health Development Policy, Ministry of Health of Indonesia. *Report: Indonesian Health Survey (IHS) 2023 in Figures. 2023, (cited 2024 August 23)* <https://www.badankebijakan.kemkes.go.id/ski-2023-dalam-angka/>
- [7] Chen, et al., "Estimated global overweight and obesity burden in pregnant women based on panel data model," *Plos One*, vol. 13, no. 8, p. e0202183, 2018. <https://doi.org/10.1371/journal.pone.0202183>
- [8] Getz, L., et al., "Maternal Pre-Pregnancy Body Mass Index and autism spectrum disorders among offspring: a population-based case-control study," *Pediatric Perinatal Epidemiol*, vol. 30, no. 5, pp. 479-487, 2018. <https://doi.org/10.1111/pep.12306>
- [9] Kent, Lisa, et al., "Global trends in prevalence of maternal overweight and obesity: A systematic review and meta-analysis of routinely collected data retrospective cohorts," *International Journal of Population Data Science*, vol. 9, no. 2, p. 06, 2024. <https://doi.org/10.23889/ijpds.v9i2.2401>
- [10] Hales, C, et al., "Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017-2018," *NCHS Data Brief*, no. 360, 2020.
- [11] Indarti, J., Susilo S.A., Hyawicaksono, P., Berguna J.S.N., Tyagitha, G.A., Ikhsan, M., *Maternal and Perinatal Outcome of Maternal Obesity at RSCM in 2014-2019. Obstetrics and Gynecology International Journal, Wiley Online Library*, vol. 2021, no. 1, 6039565, 2021. <https://doi.org/10.1155/2021/6039565>
- [12] Sudhityasa, I., *Maternal obesity statistics., Health Data Compilation* (pp. 89-102). Jakarta: Indonesian Health Data Center, 2014.
- [13] Setiawan, L. I., *A Comprehensive Midwifery care for Mrs. "L" in The Working Area of Karang Joang Health Center in Balikpapan City in 2017*, in *Repository Poltekkes-Kaltim, 2017*. <http://repository.poltekkes-kaltim.ac.id/id/eprint/908>
- [14] Gorontalo, *Prevalence of obesity in Gorontalo. Health Statistics Report*, 2018, 45-58.
- [15] Wardoyo, A.V, Ikhssani, A., *Literature Review, Maternal Obesity: Effects on Mother and Baby. Journal of Maternal and Child Health Sciences (JMHS)*, vol.1, No.2, 41-46, 2021. <https://doi.org/10.36086/maternalandchild.v1i2.1015>
- [16] Mariona, F. G., "Perspectives in obesity and pregnancy," *Women's Health*, vol. 12, no. 6, pp. 523-532, 2016. <https://doi.org/10.1177/1745505716686101>
- [17] Krakowiak P, Walker CK, Bremer AA, Baker AS, Ozonoff S, Hansen RL, et al. "Maternal metabolic conditions and risk for autism and other neurodevelopmental disorders," *Pediatrics*, vol. 129, no. 5, pp. e1121-e1128, 2012. <https://doi.org/10.1542/peds.2011-2583>
- [18] Sargowo, D., *Endothelial Dysfunction, Universitas Brawijaya Press*, 2015, pp. 54-60. ISBN: 978-602-203-805-4
- [19] Catalano, P. M., & Shankar, K., "Obesity and pregnancy: mechanisms of short term and long-term adverse consequences for mother and child," *BMJ Online Journal*, 1-40, 2017. <https://doi.org/10.1136/bmj.j1>
- [20] Sesa, I.G.A.A. I., Manu, T. T., Inayati, N., Diarti, M. W., Tatontos, E.Y., *Effect of Gestational Age on Urinary Protein by Dipstick Method (Carik Celup). Journal of Indonesia Laboratory Students (JILTS)*, vol. 2, no. 2, pp. 1-6, 2023. <https://jilts.poltekkes-mataram.id/index.php/home/article/view/30>
- [21] Bahreynian, M., Qorbani, M., Khaniabadi, B. M., Motlagh,

- M. E., & Safari, O., "Association between Obesity and Parental Weight Status in Children and Adolescents," *Journal of Clinical Research in Pediatric Endocrinology*, vol. 9, no. 2, pp. 111–117, 2017. <https://doi.org/10.4274/jcrpe.3790>
- [22] Sri, N. K., Putri, E., Relationship Between Maternal Age and Weight Gain During Pregnancy in Karanganyar District, *Jurnal Ilmiah Maternal*, vol. 2, no. 4, pp. 255–258, 2018. https://ejournal.stikesmhk.ac.id/index.php/jurnal_ilmiah_maternal/article/view/704
- [23] Slamet, "Relationship between Body Mass Index (BMI) and Glomerulus Filtration Rate Estimation in Overweight Students at the Health Analyst Department of Pontianak Health Polytechnic," *Journal Teknologi Kesehatan Borneo*, vol. 2, no. 1, pp. 27–33, 2021. <https://jtk.poltekkes-pontianak.ac.id/index.php/JTKB/article/view/32/20>
- [24] Natalia, J. R., Obstetri, B., Kedokteran, F., & Lampung, U., "The Impact of Maternal Obesity on Fetal Weight," *Medula*, vol. 10, no. 3, pp. 539–544, 2020.
- [25] Kominiarek, M. A., & Peacman, A. M., "Gestational Weight Gain," *American Journal of Obstetrics & Gynecology*, vol. 217, no. 6, pp. 642–651, 2018. <https://doi.org/10.1016/j.ajog.2017.05.040>
- [26] Hukom, E. H., Idris, I., & Sinrang, W., "Comparison of Endothelin-1 Levels in Pregnant Obese and Non-Obese Wistar Rats," *Journal Inovasi Kesehatan*, 1(October), pp. 31–35, 2019. <http://stikessorong.ac.id/ojs/index.php/ik>
- [27] Jenkins, H. N., Rivera-gonzalez, O., Gibert, Y., & Speed, J. S., "Endothelin-1 in the Pathophysiology of Obesity and Insulin Resistance," *Obesity Reviews*, vol. 21, no. 12, p. e13086, 2020. <https://doi.org/10.1111/obr.13086>
- [28] Seeger, T., Chen, C., Karakikes, I., & Wu, J. C., "30-Cardiac Remodeling and Regeneration," In *Cardiac Electrophysiology: From Cell to Bedside (Seventh Edition)* 2018, pp. 284–292. <https://doi.org/10.1016/B978-0-323-44733-1.00030-4>
- [29] Miguel, C. De, Speed, J. S., Kasztan, M., Gohar, E. Y., & Pollock, M., "Endothelin-1 and the kidney: new perspectives and recent findings," *Current Opinion in Nephrology and Hypertension*, vol. 25, no. 1, pp. 35–41, 2016. <https://doi.org/10.1097/MNH.0000000000000185>
- [30] Basile, D. P., Anderson, M. D., & Sutton, T. A., "Pathophysiology of Acute Kidney Injury," *Journal National Institute of Health*, vol. 2, no. 2, pp. 1303–1353, 2014. <https://doi.org/10.1002/cphy.c110041>
- [31] Lam, C., & Karumanchi, S. A., "Pregnancy and the Kidney," In *Textbook of Nephro-Endocrinology*; Sains Direct, pp. 7–8, 2009. <https://doi.org/10.1016/B978-0-12-373870-7.00030-2>
- [32] Utami, D. F., Idris, I., Arsyad, A., Yustisia, I., Aryandi, A., & Husni, M., Analysis of urinary endothelin-i levels in obese late adolescents. *Journal Profesi Medika*, vol. 16, no. 2, pp. 164–168, 2022.
- [33] Juan, C., Chang, C., Lai, Y., Ho, L., Chang, C., & Lai, Y., "Endothelin-1 induces lipolysis in 3T3-L1 adipocytes," *American Journal of Physiology-Endocrinology and Metabolism*, vol. 288, no. 6, pp. E1146–E1152, 2005. <https://doi.org/10.1152/ajpendo.00481.2004>
- [34] Kostov, K., "Circulating Levels of Endothelin-1 and Big Endothelin-1 in Patients with Essential Hypertension," *Pathophysiology*, vol. 28, no. 4, pp. 489–495, 2021. <https://doi.org/10/3390/pathophysiology28040031>
- [35] Saleh, L., Verdonk, K., Visser, W., Meiracker, A. H. Van Den, & Danser, A. H. J., "The emerging role of endothelin-1 in the pathogenesis of pre-eclampsia," *Therapeutic Advances in Cardiovascular Disease*, vol. 10, no. 5, pp. 282–293, 2016. <https://doi.org/10.1177/1753944715624853>
- [36] Irmayanti, "The Effect of Calcium Administration on Changes in Blood Pressure and ET-1 Cadres in Pregnant Women with Preeclampsia," Thesis: Repository Unhas, 2019. <http://repository.unhas.ac.id:443/id/eprint/4887>
- [37] Simanjuntak, M. K., "The Positive Correlation Between Endothelin-1 Levels and Score Of Roll Over Test On Preeclampsia," Thesis: Hasanuddin University, 2020, pp. 1–30.
- [38] Syarifuddin, Purnamasari, A., & Sukmawati, "Comparison of Endothelin-1 Levels as an Indicator of Vascular Dysfunction on Obese and Non-Obese Wistar Rats," *Journal UIN Alauddin*, pp. 1–7, 2017. <https://journal.uin-alauddin.ac.id/index.php/biotek/article/download/5092/pdf/>