

# THE RISKS OF HYPERTENSION IN PREGNANT WOMEN: A META-ANALYSIS

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## ABSTRACT

**Background:** Hypertensive disorders in pregnancy were a global public health problem. Hypertension is a significant contributor for pregnant women to experience life-threatening complications during pregnancy and delivery or in the postpartum period. This study aimed to determine the risk factors for hypertension in pregnant women, with a meta-analysis of the primary study conducted by previous authors.

**Subjects and Method:** This study was a systematic review and meta-analysis. Online articles from 2011 to 2021 were searched from databases, including PubMed, MEDLINE, BASE, and ProQuest. The PICO was as follows. Population: pregnant women. Intervention: hypertension before pregnancy, family history of hypertension and diabetes in the mother. Comparison: without hypertension before pregnancy, without a family history of hypertension and diabetes in the mother. Outcome: hypertension. Keywords "hypertension," "history of hypertension in the family," "diabetes," "risk factors," and "pregnant women." Articles were analyzed using the Review Manager 5.3 application.

**Results:** A total of seven articles from China, Ethiopia, Jordanian, Brazil, Pakistan, and Ghana were included in the meta-analysis. The data showed that pregnant women with chronic hypertension before pregnancy (OR= 5.05; 95% CI= 2.78 to 9.17; p= 0.001), diabetes (OR= 3.15; 95% CI= 1.63 to 6.10; p= 0.001), and a family history of hypertension (OR= 3.45; 95% CI= 2.05 to 5.80; p= 0.001) were at risk of developing hypertension during pregnancy.

**Conclusion:** Chronic hypertension before pregnancy, diabetes, and a family history of hypertension are risk factors hypertension during pregnancy.

**Keywords:** hypertension, family history, diabetes, risk factors, pregnant women

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## BACKGROUND

The World Health Organization (WHO) reports that globally, 14.0% of maternal deaths are related to pregnancy or gestational hypertensive disorders (Say et al., 2014). Gestational hypertensive disorders are a major cause of morbidity and mortality affecting 3-10% of all pregnancies. Gestational hypertensive disorders

can also lead to preeclampsia and eclampsia, which contribute up to 16% as a cause of maternal death in developed countries (Duley, 2009; Khan et al., 2006; Wallis et al., 2008).

Hypertensive disorders of pregnancy consist of hypertension induced or caused by pregnancy (gestational hypertension and preeclampsia) as well as hypertension that was present

before pregnancy (chronic hypertension). Pregnancy-induced hypertension is defined as an increase in blood pressure after 20 weeks of gestation, the difference with preeclampsia is the presence of proteinuria (Brown et al., 2001; Staley et al., 2015). Hypertensive disorders of pregnancy represent a group of conditions characterized by high blood pressure during pregnancy, proteinuria and, in some cases, seizures. If not treated immediately, this condition can lead to death. Worldwide, hypertensive disorders of pregnancy can complicate 5-10% of all pregnancies (Agrawal and Fledderjohann, 2016).

Women with a history of hypertensive disorders in pregnancy also have an increased risk of cardiovascular disease, stroke, and type II diabetes later in life. Babies of mothers with hypertension are more likely to show intrauterine growth restriction, premature birth, and low birth weight, this is due to decreased blood supply to the placenta (Barton et al., 2001; Feig et al., 2013; Heida et al., 2013; Umesawa and Kobashi, 2017; Wilson et al., 2003; Yesil et al., 2016). Pregnant women are susceptible to stress, which can affect the state of fetal growth in the womb (Handayani et al., 2020). Most previous studies on women with hypertensive disorders in pregnancy have shown that there is a relationship with an increased incidence of stillbirth (Ahmad and Samuelsen, 2012; Ananth & Basso, 2010; Bellizzi et al., 2017; Harmon et al., 2015; Keyes et al., 2003; Villar et al., 2006; Ye et al., 2009).

Specifically, nulliparity, old age, obesity, family history of hyperten-

sion, history of hypertensive disorders of previous pregnancy in multiparous women, personal/family history of chronic hypertension/ diabetes mellitus, high energy diet, gestational diabetes, mental stress during pregnancy, long interval between pregnancy, lower socioeconomic status and inadequate antenatal care were associated with a higher risk of developing hypertensive disorders of pregnancy in most studies (Atkinson et al., 1998; Brantsaeter et al., 2009; Conde-Agudelo and Belizán, 2000; Dalmáz, Santos et al., 2011; Guerrier et al., 2013). Based on the description of the problems above, this study aims to determine the risk factors for the incidence of hypertension in pregnant women.

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## **SUBJECTS AND METHOD**

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### **1. Study Design**

The design of this study was a systematic review and meta-analysis. The articles used in this study were obtained from several online databases namely PubMed, MEDLINE, BASE, and ProQuest between 2011 and 2021. The keywords to search for articles were "hypertension", "history of hypertension in family", "diabetes", "risk factors", and "pregnant women".

### **2. Inclusion Criteria**

The inclusion criteria of this study were: full-text articles with a case-control study design. The research subjects were pregnant women. Original research papers. This research uses multivariate logistic regression analysis method.

### **3. Exclusion Criteria**

The exclusion criteria for this study were: articles published in languages

other than English and Indonesian. Review papers. Research data is incomplete or not available. Articles before 2011.

#### 4. Operational Definition of Variables

Hypertension in pregnancy was defined as a systolic blood pressure greater than or equal to 140 mmHg and/or a diastolic blood pressure greater than or equal to 90 mmHg on two examinations at least 6 hours apart after the fifth month of pregnancy for pregnancy-induced hypertension or before pregnancy/ before 20 weeks gestation for chronic hypertension.

#### 5. Instrument

Articles included in this study must meet the inclusion criteria and have been reviewed using a critical

appraisal in accordance with the research design of each article..

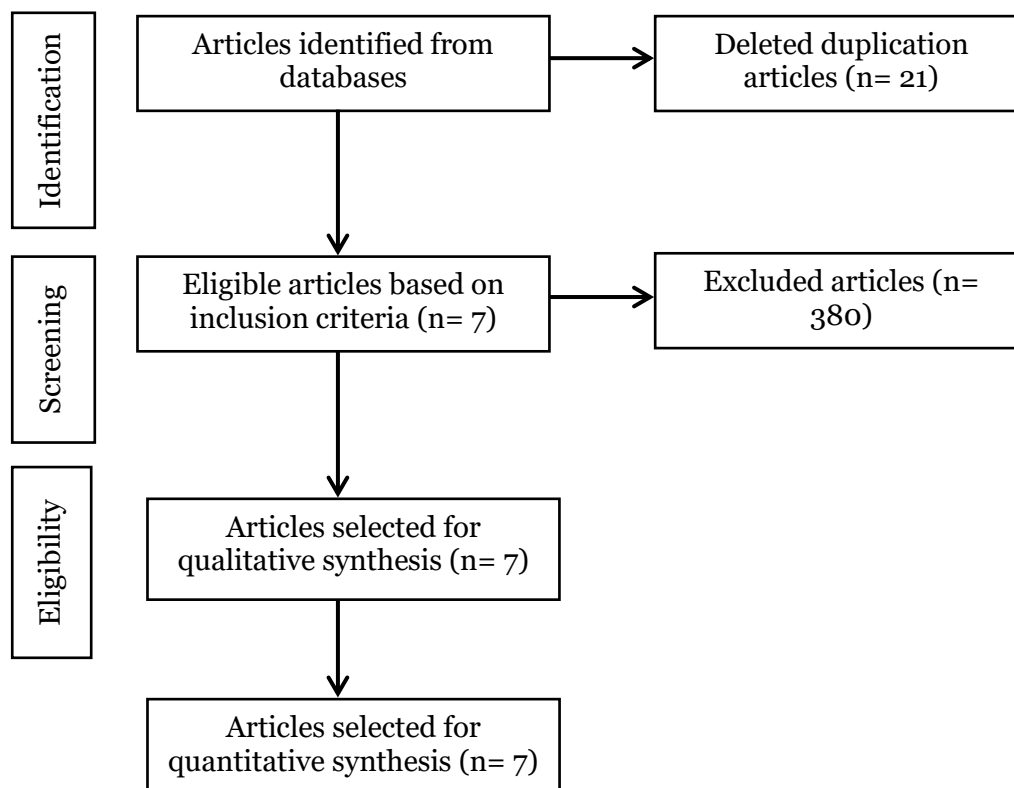
#### 6. Data Analysis

The data in the study were analyzed using the Review Manager application (RevMan 5.3).

## RESULTS

### 1. Sample Characteristics

There are a total of 386 articles searched from the PubMed, MEDLINE, BASE, and ProQuest online databases. There were a total of 7 articles that met the inclusion criteria and were processed in qualitative and quantitative synthesis. The characteristics of each article included in the qualitative synthesis have been described in table 1. There are 3 risk factors that were analyzed using the review manager application.



**Figure 1. PRISMA Diagram**

**Table 1. Description of the primary studies included in the meta-analysis primary studies**

No	Author (year)	Study Design	Number of subjects	P (Population)	I (Intervention)	C (Comparison)	O (Outcome)	aOR (95% CI)
1.	Hu et al., (2015)	Case-control	373 hypertensive cases and 507 normotensive controls	pregnant women	Family history of hypertension	Mothers who do not have a family history of hypertension	Maternal hypertension	6.18 (2.37 to 16.14)
2.	Hinkosa et al., (2020)	Case-control	Case (243) and for control (534) the total sample size was 777.	pregnant women	Family history of hypertension, maternal diabetes, maternal hypertension before pregnancy	Mothers who do not have a family history of hypertension, do not have diabetes, do not have hypertension before pregnancy	Maternal hypertension	5.04 (2.66 to 9.56), 5.03 (1.59 to 15.89), 3.81 (1.69 to 8.58)
3.	Suleiman, (2013)	Case-control	184 Jordanian pregnant patients with hypertensive disorders and 172 age-matched control subjects	pregnant women	Family history of hypertension, maternal diabetes, maternal hypertension before pregnancy	Mothers who do not have a family history of hypertension, do not have diabetes, do not have hypertension before pregnancy	Maternal hypertension	4.00 (1.62 to 9.11), 4.11 (1.84 to 13.02). 6.98 (2.07 to 25.08)
4.	Dalmáz et al., (2011)	Case-control	161 patients with hypertensive disorders and 169 control	pregnant women	Family history of hypertension, maternal diabetes, maternal hypertension before pregnancy	Mothers who do not have a family history of hypertension, do not have diabetes, do not have hypertension before pregnancy	Maternal hypertension	3.88 (1.77 to 8.46), 3.87 (1.22 to 12.27), 7.05 (1.99 to 24.93)
5.	Mubarik et al., (2019)	Case-control	549(27.45%) were hypertensive cases and 1451(72.55%) were normotensive	pregnant women	Family history of hypertension, maternal diabetes	Mothers who do not have a family history of hypertension, do not have diabetes	Maternal hypertension	1.50 (1.07-2.11), 1.49 (1.05 to 2.12)

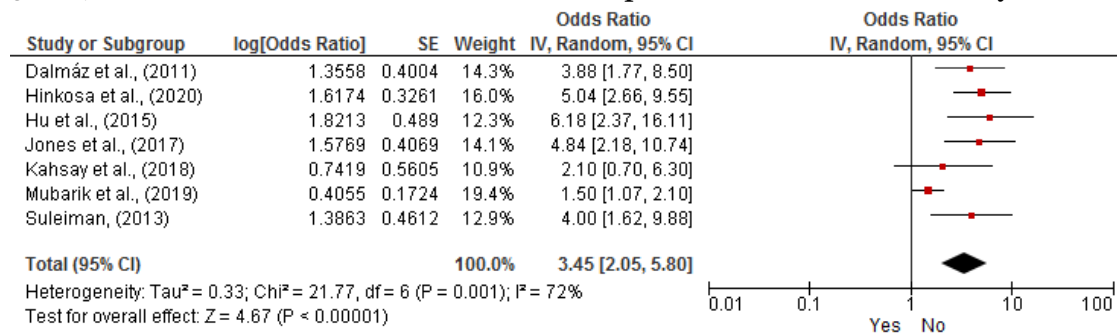
6.	Kahsay et al., (2018)	Case-control	controls. 110 cases and 220 controls who were pregnant women.	pregnant women	Family history of hypertension, maternal diabetes	Mothers who do not have a family history of hypertension, do not have diabetes,	Maternal hypertension	2.1 (0.7 to 6.4), 5.4 (1.1 to 27.0)
7.	Jones et al., (2017)	Case-control	108 cases and 108 controls	pregnant women	Family history of hypertension	Mothers who do not have a family history of hypertension	Maternal hypertension	4.84 (2.18-10.73)

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## 1. Family History of Hypertension

Pregnant women who have a family history of hypertension have a 3.45 times risk of gestational hypertension compared to pregnant women who do not have a family history of hypertension (aOR = 3.45; 95% CI = 2.05 to 5.80), and the results were statis-

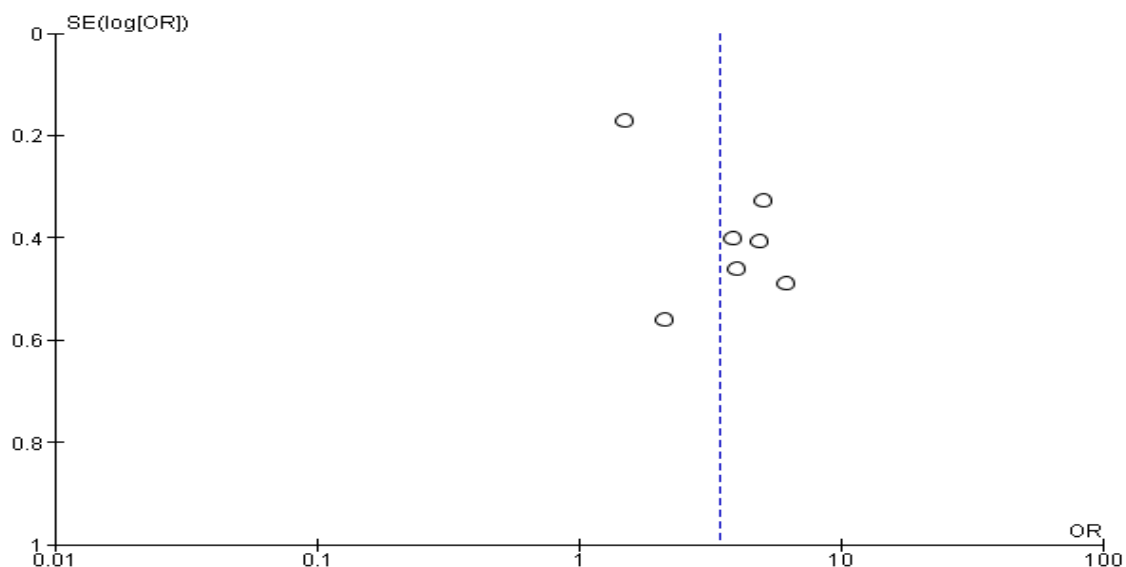
tically significant ( $p < 0.001$ ). The heterogeneity of the research data shows  $I^2 = 74\%$  so that the distribution of the data is declared heterogeneous (random effect model) (graph 1). The asymmetrical distribution of circles in the funnel plot (graph 2) indicates that there is publication bias in this analysis.



**Figure 1. Forest plot of the variable history of hypertension in the family**

The forest plot in Figure 1 shows that mothers with a family history of hypertension have a 3.45 times risk of developing hypertension during pregnancy compared to mothers without a family history of hypertension (aOR = 3.45; 95% CI = 2.05 to 5.80), and

these results are generally statistically significant ( $p < 0.001$ ). The heterogeneity of the research data shows  $I^2 = 72\%$  so that the distribution of the data is declared heterogeneous (random effect model).



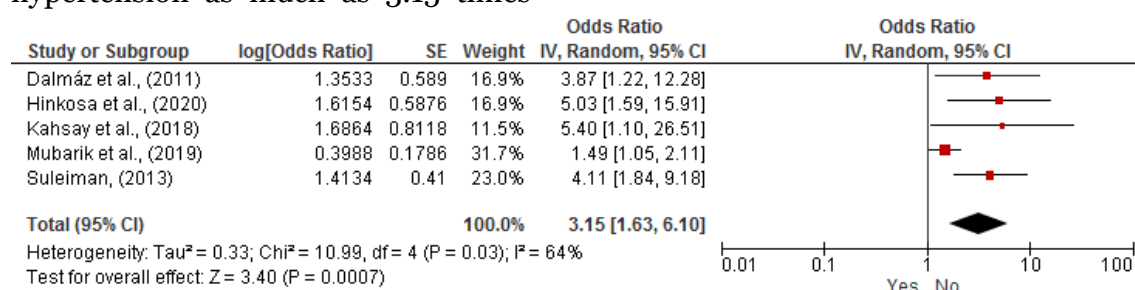
**Graph 2. Funnel plot of the history of hypertension in the family**

The funnel plot in Figure 2 shows publication bias with an over-estimated effect characterized by an asymmetric distribution between the right and left plots. There are two plots on the right and five plots on the left. The plot on the right side of the graph has a standard error (SE) between 0 and 0.6. The plot on the left side of the graph has a standard error (SE) between 0.2 and 0.6.

## 2. Diabetes in Mother

Pregnant women with diabetes were at risk of developing gestational hypertension as much as 3.15 times

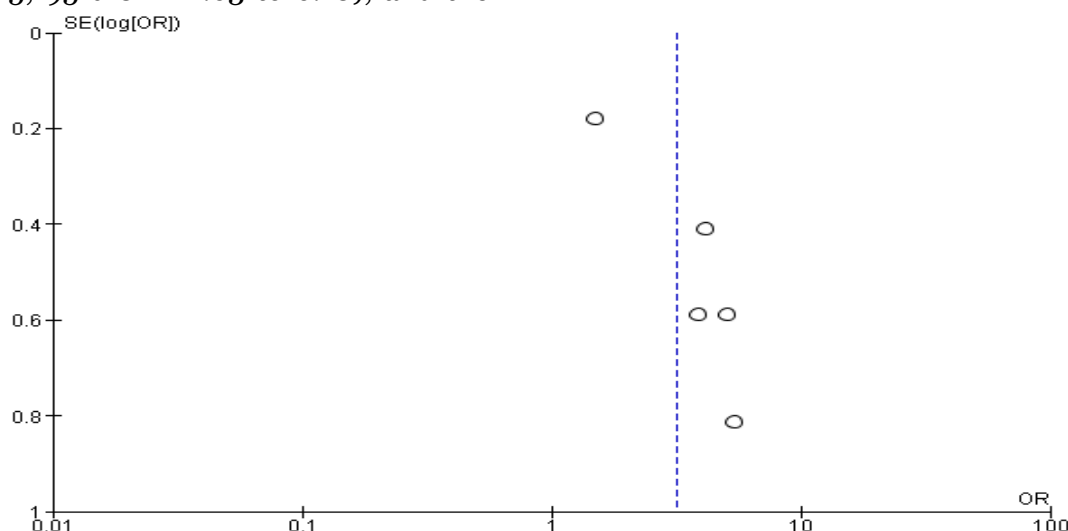
compared to pregnant women who did not have diabetes (aOR= 3.15; 95% CI= 1.63 to 6.10), and the results were statistically significant ( $p=0.007$ ). The heterogeneity of the research data shows  $I^2=64\%$  so that the distribution of the data is declared heterogeneous (random effect model). The asymmetrical distribution of circles in the funnel plot (graph 4) indicates that there is publication bias in this analysis.



**Figure 3. Forest plot of maternal diabetes variables**

The forest plot in Figure 3 shows that mothers with diabetes had a 3.15 times risk of developing hypertension during pregnancy compared to mothers without diabetes (aOR = 3.15; 95% CI = 1.63 to 6.10), and the

results were statistically significant ( $p < 0.007$ ). The heterogeneity of the research data shows  $I^2 = 64\%$  so that the distribution of the data is declared heterogeneous (random effect model).



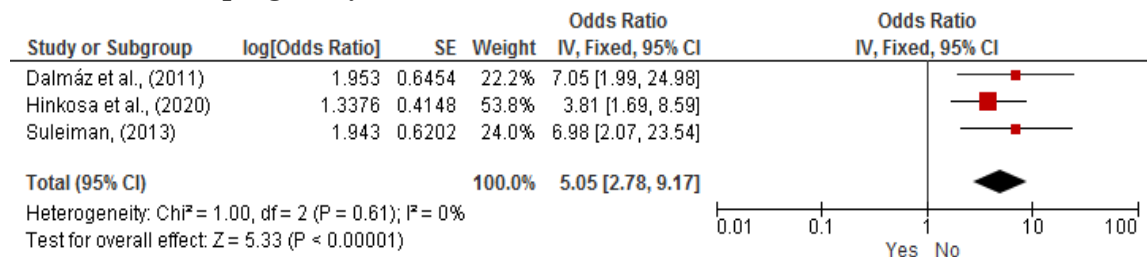
**Figure 4. Funnel plot of maternal diabetes**

The funnel plot in Figure 4 shows publication bias with an overestimated effect characterized by an asymmetric distribution between the right and left plots. There is one plot on the right and four plots on the left. The plot on the right side of the graph has a standard error (SE) between 0 and 0.2. The plot on the left side of the graph has a standard error (SE) between 0.4 and 1.0.

### 3. Chronic Hypertension in Mother

Pregnant women who had hypertension before pregnancy had a 5.05

times higher risk of gestational hypertension than pregnant women without hypertension before pregnancy (aOR= 5.05; 95% CI= 2.78 to 9.17), and the results were statistically significant ( $p < 0.001$ ). The heterogeneity of the research data shows  $I^2 = 0\%$  so that the distribution of the data is declared homogeneous (fixed effect model) (Figure 5). The asymmetrical distribution of circles in the funnel plot (Figure 6) indicates that there is publication bias in this analysis.

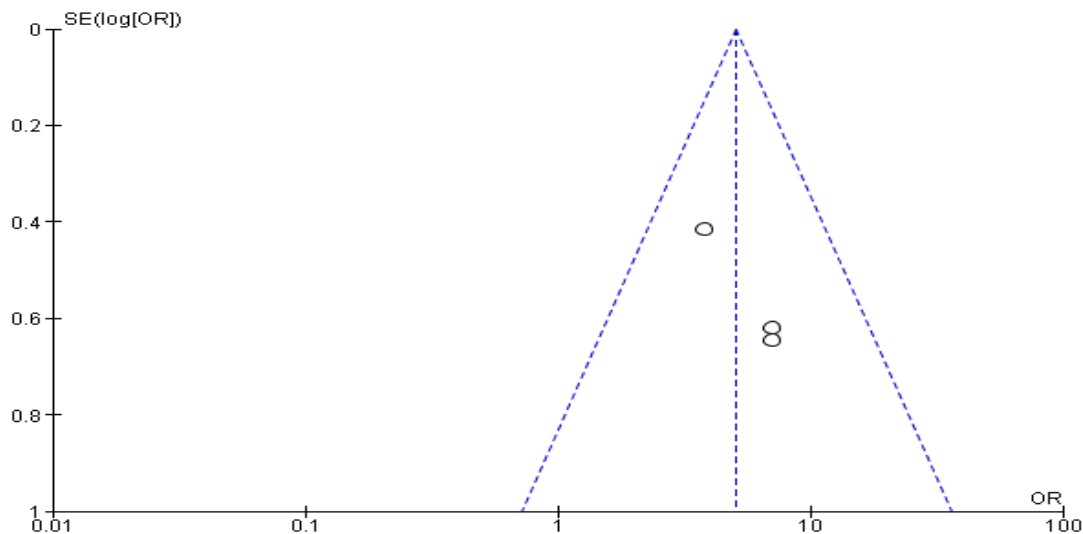


**Figure 5. Forest plot of disease variables maternal hypertension before pregnancy**

The forest plot in Figure 5 shows that mothers with maternal hypertension before pregnancy had 5.05 times the risk of developing hypertension during pregnancy compared to mothers who did not have hypertension before pregnancy (aOR =

5.05; 95% CI = 2.78 to 9.17), and the results were statistically significant ( $p < 0.001$ ). The heterogeneity of the research data shows  $I^2 = 0\%$  so that the distribution of the data is declared homogeneous (fixed effect model).





**Figure 6. Funnel plot of disease variables maternal hypertension before pregnancy**

The funnel plot in Figure 6 shows publication bias with an over-estimated effect characterized by an asymmetric distribution between the right and left plots. There is one plot on the right and two plots on the left. The plot on the right side of the graph has a standard error (SE) between 0.4 and 0.6. The plot on the left side of the graph has a standard error (SE) between 0.6 and 0.8.

## DISCUSSION

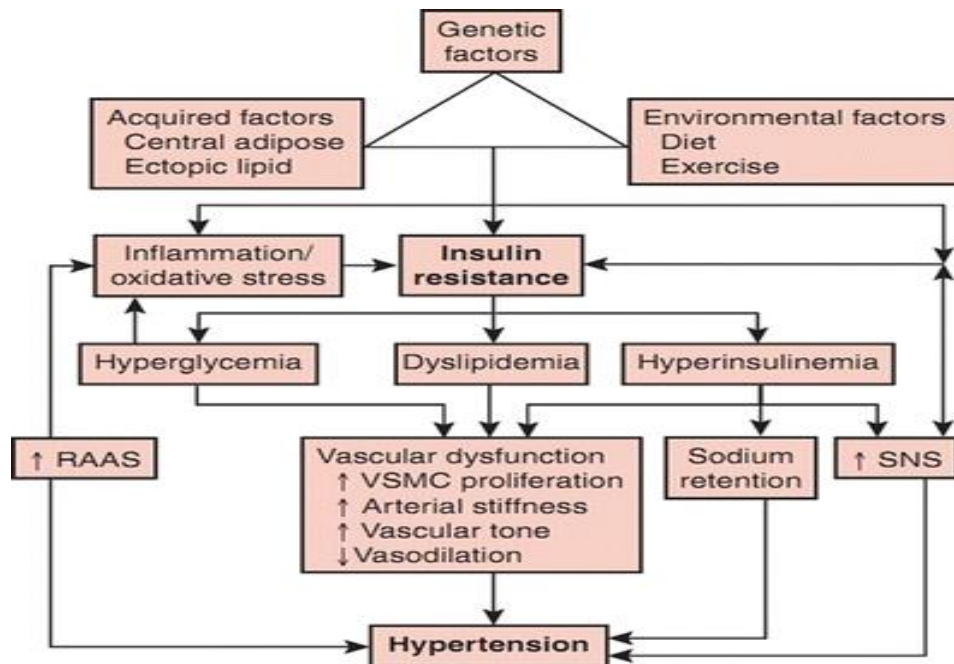
The results of the meta-analysis in this study indicate that there is a relationship between a history of hypertension in the mother's family and the risk of developing gestational hypertension. This is in accordance with Duckitt and Harrington (2005), which states that a positive family history of chronic hypertension is a risk factor for gestational hypertension. According to Mütze et al. (2008) the relationship between the two is influenced by genetic components in pathophysiological disorders associated with hypertension. Based on

the theory put forward by adam et al., (2011) that pregnant women who have a history of hypertension in the family are more prone to experiencing hypertension during pregnancy.

This meta-analysis study states that pregnant women who have diabetes are more prone to developing gestational hypertension than pregnant women who do not have diabetes. Bryson et al. (2003) explained the same thing, that gestational diabetes mellitus was significantly associated with hypertension disorders during pregnancy. According to Jensen et al. (2000) in his research, that the group of pregnant women with gestational diabetes mellitus had a statistically significant higher frequency of pregnant women with hypertension. The study by Luan et al., (2010) also states the same thing. Diabetes and hypertension share similar pathways, such as sns, raas, oxidative stress, adipokines, insulin resistance, and ppar. These pathways interact and influence each other (Figure 2). Hypertension and diabetes will have

the same result, namely the occurrence of metabolic syndrome

disorders in the body (Cheung and Li, 2012).



**Figure 2. Summary of pathophysiological mechanisms of hypertension development in diabetes mellitus. RAAS—renin system angiotensin-aldosterone; sns—sympathetic nervous system; vsmc—vascular smooth muscle cells (Mugo et al., 2007).**

The results of the analysis in this study indicate that pregnant women who had hypertension before their pregnancy had a greater risk of developing hypertension during pregnancy. The previous study by Bezerra et al. (2010) also explained the same opinion, that pregnant women who had hypertension before pregnancy were more prone to developing hypertension during their pregnancy. The results of this study are in accordance with several theories that have been put forward in several studies.

The conclusion of this study is that the risk factors for hypertension in pregnant women consist of hypertension before pregnancy, diabetes, and a family history of hypertension. There are some limitations to this

review. First, this study was limited to English-language articles, so the researcher considered the potential for publication bias even though statistical analysis did not detect publication bias. also, the researchers were not aware of any unpublished articles that met the criteria for this study. third, the subgroup analysis conducted is limited to one characteristic only, while other characteristics can be explored. Finally, there are a limited number of studies on risk factors for the incidence of hypertension in pregnant women, so further research is needed for further evidence.

#### **FUNDING AND SPONSORSHIP**

This study is self-funded.

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### ACKNOWLEDGMENT

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We thank the online database providers PubMed, MEDLINE, BASE, and ProQuest.

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### CONFLICT OF INTEREST

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There is no conflict of interest in this study.

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