

## Relationship between Anaemia during Pregnancy and Postpartum Haemorrhage .....

**Comment [S1]:** I think please add research area i.e. province or state or city of Saudi Arabia

### Abstract

**Background:** Anemia during pregnancy is an important cause of morbidity and mortality among postpartum women. The main reason for the condition is dietary Iron deficiency and the most common type of anemia found in women during pregnancy is iron deficiency anemia. Among many complications, postpartum hemorrhage is a problem linked with anemia during pregnancy. In Saudi Arabia, pregnancy and postpartum haemorrhage (PPH) is not common but still cases are reported. The present study aimed to determine its prevalence in population and to see its relationship with anemia during pregnancy.

**Methods:** It was an analytical cross sectional study in which the data was collected from women using properly designed questionnaires. The study population was women who got pregnant and delivered in main hospitals of the kingdom of Saudi Arabia. The data of respondents for demographical and clinical variables was collected and analyzed using SPSS using appropriate statistical tests.

**Comment [S2]:** Were

**Results:** 600 participants responded to the questionnaire. The mean age was 26.32 years. The prevalence of PPH among studied population was 11.9%. Anemia during pregnancy was found to be positively associated with PPH with the p value of 0.0039. Smoking history was also correlated with PPH. There was no strong association between age and increase risk of PPH.

**Comment [S3]:** Write standard deviation also

**Conclusion:** The study concluded that PPH is not common in Saudi Arabia. There is a moderate association of anemia during pregnancy and PPH. Smoking is also a positive predictor for PPH. There are some limitations in the study so there is a need of large scale study to confirm the findings in the population.

**Comment [S4]:** Please omit these sentence and add scientific or proper sentence

**Comment [S5]:** Define the term statistically? what does it mean?

**Keywords:** Anemia, hemoglobin, PPH, Iron deficiency, Pregnancy.

**Comment [S6]:** Omit this key word

### Background:

Anemia is the most common problem for pregnant women around the globe. According to world health organization (WHO), hemoglobin levels below 11g/dl in females in the course of pregnancy is considered as anemia during pregnancy

(1). According to another definition, in the first and 3<sup>rd</sup> trimester of pregnancy, hemoglobin levels below 11g/dl is considered as anemic conditions while during 2<sup>nd</sup> trimester it should be less than 10.5g/dl to be called as anemic. A number of factors contribute to this condition such as iron deficiency in food, malabsorption, excessive loss of blood, genetic or acquired haemoglobin synthesis disorder, and other medical conditions causing anemia (2). In developed countries the prevalence is upto30% while in developing countries, the prevalence of the condition is nearly 50 % (3). The mild decrease in hemoglobin is common and happens in every pregnant woman, but severe condition should be taken seriously. It also negatively affects the quality of life. For example, females with the condition have reported compromised thinking ability, tiredness, unstable moods, depression, and increased risk for infections (4, 5).

**Comment [S7]:** Referencing style modified based on JPRI

Studies have shown that anemia during pregnancy increases the risk postpartum hemorrhage (PPH), a condition in postpartum women, characterized by the excessive loss of blood (>500ml) and leading to hypovolemia (6). Although, normal bleeding after delivery is common and is expected in all postpartum women, but excess can lead to serious conditions. Statistics reveal that PPH is one of the main causes for maternal mortality around the globe. There are two Types of PPH; primary which occurs within 24 hours after deliver and secondary which occurs after 24 hours of the delivery. Some studies have found week association between anemia during pregnancy and PPH, while others strongly correlate both conditions (7, 8).

In Saudi Arabia, the maternal mortality rate is 17 per 10000 birth cases (9) and not enough research has been done to determine the risk factors. The PPH condition is not alarming, but still cases are reported on regular basis. There are not enough studies done so far and most of the work is done related to neonates and a bit less attention has been given to maternal health compared to the neonates. So we designed this study with the main aim to determine the relationship between anemia during pregnancy and the incidence of postpartum hemorrhage. Our other objectives were 1. To determine the prevalence of PPH in Saudi population. 2. To determine the relationship between smoking status and PPH. 3.To determine the relationship between age and increase incidence of PPH.

**Comment [S8]:** MMR data are not found in reference 9 research paper

**Comment [S9]:** Please re-write word

**Comment [S10]:** Clearly add specific province or state, and study sample size are not represented country

**Comment [S11]:** Omit this sentence and add to specific and clear words

### Methods:

This was an analytical cross sectional study conducted in kingdom of Saudi Arabia in 2020. The main study population was females who got pregnant and delivered from 05/08/2020 till 22/11/2020 in main hospitals of the kingdom. The information was collected using a carefully designed questionnaire. The help of clinicians and

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**Comment [S13]:** Clearly mentioned about the sampling techniques

registered gynecologists were taken while designing the questionnaire to prevent the wrong type of data collection and misinterpretation. Administrative approval was sought from the unit of biomedical ethics research committee. All the Ethical standards were followed and the approval was taken from the ethical committee of the faculty of medicine, king Abdulaziz University. Furthermore, an informed consent was signed from the participants and questionnaires were distributed among the participants. The participants who agreed to take part in the study were given enough time to review the questionnaire and if they had any query and if they did not understand any term, they were explained by the researchers before answering the questions. We used OpenEpi for sample size calculation for cross sectional studies.

**Comment [S14]:** Re-write sentence

**Comment [S15]:** Please mention about the sample size.

**Comment [S16]:** How to validated questionnaire

**Comment [S17]:** Self-administrative questionnaire or structured questionnaire clarify and proper study tool defined

**Comment [S18]:** How to calculated sample size of the study and mention proper methods of sample size calculation in this research and sample size process included methodology part of research

**Comment [S19]:** Re-write sentence

The respondents' data collected was demographic characteristics such as age and nationality. Clinical characteristics data collected was anemia status, anemia history, diabetes history, and uterine fibroid status, history of uterine Atony and polyhydramnios, PPH history, time of bleeding after delivery. Other information collected were age of menarche, duration of menstruation, hemoglobin levels, history of diabetes, and other maternal characteristics. The collected data was verified independently by two researchers before doing any analysis.

### Statistical Analysis

The collected data was organized and cleaned for any outliers. It was then entered into SPSS version 20 and analyzed using appropriate statistical tests. For anemia during pregnancy, 10.5g/dl cut off was used because it is considered as standard by WHO. First, descriptive analysis was done and presented as mean + standard deviations. To determine the relationship between anemia during pregnancy and PPH, simple linear regression was applied on data. Furthermore, Kruskal Wallis and Wilcoxon rank tests were performed during bivariate analysis. Also, the association of smoking status with PPH and age with PPH was calculated using regression analysis.

**Comment [S20]:** How to manage and clean research data, please clearly mention this part

**Comment [S21]:** Add reference

### Results:

Sample size calculation predicted 700 sample size for the study. We got responses from 600 participants. From bases line characteristics, the mean age was 26.32 years with standard deviation of 7.89 years. Regarding nationality of the respondents, 93.7% were Saudis and 6.3% were non Saudis and residents of Saudi Arabia. 13% had age of menarche below 12 years, 61.3% between 12-15 years, and 25.7 % above 15 years. In response to the duration of menstruation, 7.5 % had less than 5 days, 80.3 % had 5-7 days and 12.2 % had more than 7 days. 82.5%

**Comment [S22]:** This part clearly defined in methodology part (sample size calculation part) and non-response rate also mention

were nonsmokers, 13.7% were active smokers and 3.8% of respondents were X-smokers. Further analysis revealed that smokers had more chances of PPH, although the results were statistically non-significant (P=0.396).

**Comment [S23]:** Change other word and omit this word

#### Base line characteristics

<b>Age</b>	26.32 years
<b>Nationality</b>	93.7% Saudis 6.3% non-Saudis
<b>Blood group</b>	25.7% had A+ blood group, 46.7 O+, 9.7% B+, 6.8% AB+, 3.8% A-, 5.7% O-, 0.7% B- and 1% of the respondents had AB- blood group
<b>Age of menarche</b>	13% below 12 years, 61.3% between 12-15 years 25.7 % above 15 years
<b>Duration of menstruation</b>	7.5 % < 5 days, 80.3 % 5-7 days 12.2 % > 7 days
<b>Smoking status</b>	82.5% nonsmokers 13.7% active smokers 3.8% X-smokers

**Comment [S24]:** Table no. add and follow the JPRI guideline properly

**Comment [S25]:** Clearly mentioned it as mean age

**Table 1:** The above table summarizes the base line characteristics of respondents

Regarding diabetes status, 94.7 were non diabetic and 5.3 had the diabetes. Moreover, 25.7% had A+ blood group, 46.7 O+, 9.7% B+, 6.8% AB+, 3.8% A-, 5.7% O-, 0.7% B- and 1% of the respondents had AB- blood group. When asked about uterine fibroids, 93.8% told they did not have the condition and 6.2% of respondents had the condition. Also, 96.2% did not ever have uterine atony and 3.8 % had that condition. 9.7% of the women were found with polyhydramnios and 90.3 % did not have that disorder. We also took the anticoagulant medication history like aspirin. 9.5 % of the respondents were having the aspirin while 90.5 were never took the anticoagulant medication. Furthermore, 98.7% did not have any cardiac disease and only 1.3 % were cardiac patients.

#### Clinical Characteristics

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<b>Diabetic status</b>	94.7% non-diabetic 5.3% diabetic
<b>uterine fibroids</b>	93.8% negative 6.2% positive
<b>uterine Atony</b>	96.2% Negative 3.8 % Positive
<b>Polyhydramnios</b>	9.7% Positive 90.3 % Negative
<b>Anticoagulant medication history</b>	9.5 % positive 90.5% negative
<b>cardiac disease</b>	98.7% Negative 1.3 % Positive

**Table 2:** The above table summarizes the Clinical characteristics of respondents

Our main question was anemia during pregnancy; 46.2% of the respondents had anemia during pregnancy while 53.8 % did not have. When analyzed with the PPH, it was found that anemia during pregnancy was statistically correlated with PPH with the p value of 0.0039. Furthermore, 46.2 % of the respondents who had anemia during pregnancy, 11% had the condition in first trimester, 11.8% in 2<sup>nd</sup> trimester and 23.3% had this condition in the 3<sup>rd</sup> trimester. Regarding PPH diagnosis question, 277 respondents answered it. Out of that 277, 11.9% were diagnosed with PPH and 88.1% were never diagnosed with that condition. Those who had PPH, 90.9% were diagnosed with primary PPH; occurring within 24 hours of delivery and 9.1% had secondary PPH; occurring after 24 hours of delivery.

<b>Anemia and PPH related characteristics</b>	
<b>Anemia during pregnancy</b>	46.2% Yes 53.8 % No
<b>Trimester in which anemia diagnosed</b>	11% in 1 <sup>st</sup> trimester, 11.8% in 2 <sup>nd</sup> trimester and

**Comment [S27]:** Table no. add and follow the JPRI guideline properly

	23.3% in 3 <sup>rd</sup> trimester
<b>PPH diagnosis</b>	11.9% were diagnosed with PPH
	88.1% were never diagnosed with that condition
<b>Type of PPH</b>	90.9% were primary PPH
	9.1% had secondary PPH

**Table 3:** The above table summarizes the anemia and PPH related characteristics of respondents

One of the aims was to determine the prevalence of PPH in Saudi population and it was found to be 11.9%. Furthermore, when age was compared with high incidence of age PPH, no statistical association was found. Age had no effect on the incidence of PPH (P=0.1259).

### Discussion:

This study was conducted with the main aim to determine the relationship between anemia during pregnancy and PPH in kingdom of Saudi Arabia. We found that there is a positive association between anemia during the pregnancy and blood loss at delivery and this is one of the significant features of this study. The same findings have also been found in similar studies conducted in other parts of the world (10, 11, and 12). For example, a study found positive association between anemia during pregnancy and PPH among women in India. Also, another study strong correlation between anemia in pregnancy and PPH in Southern Africa. Other studies did not find any positive correlation, and there can be number of reasons for the results.

Researchers have proposed various mechanisms involved in the development of PPH (13, 14). One of the hypotheses is that the blood loss causes loss of uterine muscle strength resulting in reduced blood flow (15). The factors cause inefficient contractions for uterine muscles and increased blood loss especially when coupled with iron deficiency in the body. Furthermore, it also leads to mortality of mothers in cases where the condition is reported later or there are delays in the transfer of patients to the hospitals (16).

Furthermore, we also found that smoking is also a positive predictor for PPH. Similar findings were also reported by some studies (17). While other studies did

**Comment [S28]:** Better to show Bivariate and regression analysis in Table.

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not find any correlation between smoking history and increased chances of PPH (18).

We did not find any correlation between age and increase incidence of PPH. Although some studies have concluded that the chances of PPH is more in older age women compared to younger (19) but we did not find any such association in our data. There can be a number of reasons for this discrepancy in our results, most important being the low age of respondents. The average age of our respondents was 26.32 while the study cited above had average age of 30.29 (20).

There are several limitations in this study which should be mentioned. The first one is the sample size. The study sample is not large enough to fairly conclude about the whole population of Saudi Arabia. Second important limitation is the direct examination of respondents. We took the data by asking questions using a properly designed questionnaire which has drawback of respondents not explaining everything in detail and thus missing important data points. Furthermore, there were not enough questions to determine the cause of anemia. For example, we did not ask about their dietary habits if they were taking enough iron or other related supplements. Also, we had a large loss of follow up on many of the important questions. We lost about half of the respondents for the answers of questions.

Despite the limitations and lack of many important factors, our study has confirmed the suspected link between the anemia during pregnancy and PPH. The authorities should take measures to prevent anemia during pregnancy to protect mothers from PPH.

### Conclusion:

We can conclude, based on the findings of this study that PPH is not highly prevalent and anemia during pregnancy is one of the risk factors for postpartum hemorrhage in Saudi Arabia. Furthermore, smoking status also contribute positively to the condition. There are some limitations in the study so there is a need of a large scale study with more sample size, recruiting respondents from all areas and demographics backgrounds, and controlling confounding variables to confirm the findings of this study in Saudi population.

### Declarations

### Ethics approval and consent to participate

Not applicable

### Consent for publication

**Comment [S31]:** Please work out and improve the quality of English.

**Comment [S32]:** Re-write this sentence and conclusion part

**Comment [S33]:** This part included in separate part of the research i.e. limitation or delimitation of the study

**Comment [S34]:** I know this is the laboratory based research and this type of research are more human sensitive so please appropriately include ethical approval and consent of participants in this research

Not applicable

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### Availability of data and material

Data sharing not applicable to this article as no data-sets were generated or analyzed during the current study

**Comment [S37]:** Without data set how you can analyzed and prepare the manuscript.

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