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## The Usage of Tocolytic Drugs in Pregnant Women With the Threat or Preterm Labor in PKU Muhammadiyah Gamping Hospital Yogyakarta

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### Keywords

PKU Muhammadiyah Gamping Hospital; Partus Prematurus Imminens; Tokolitik Drugs.

### Abstract

Partus Prematurus Imminens (PPI) is a threat to pregnancy caused by contractions in the uterus at a gestational age that has not reached 37 weeks, or what is commonly called preterm labour. According to the WHO, there are around 10-11% of preterm births in the world each year, while in Indonesia, the WHO explains that there are around 16% of preterm deliveries, which places Indonesia in fifth place with the largest preterm deliveries in the world. Management and prevention efforts with tocolytic therapy is a therapy used to suppress uterine contractions. This research used analytic descriptive observational with a cross-sectional approach where these observations were made within the past 5 years. The sample in this study was conducted on pregnant women who experienced the threat of preterm labour. This research found that most of the samples recovered as many as 23 (95.8%) people, and the most used drug was Nifedipine, with a recovery status of 12 (50.0%) people, while the rest were Hystolan. However, there was no significant relationship between drug use and recovery in pregnant women with imminent premature labour, as shown by the Fisher Exact Test,  $p$  value  $> 0.05$ . Tocolytic drugs are effective to be given to pregnant women with Partus Prematurus Imminens (PPI). However, there was no significant relationship between the drug (Nifedipine and Hystolan) and the recovery of pregnant women with imminent preterm labour (PPI) at PKU Muhammadiyah Gamping Hospital, Yogyakarta.



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### 1. Introduction

Partus Prematurus Imminens (PPI) is a threat to pregnancy caused by contractions in the uterus at a gestational age that has not reached 37 weeks or is commonly referred to as a premature copy (Fitria, Prawita, & Yana, 2021). Low birth weight babies often follow this. Low birth weight infants cause significant neonatal morbidity and mortality events. Preterm labour is a major threat worldwide for mothers who are experiencing pregnancy; preterm labour can occur if the baby is born less than 32 weeks or weighs less than 1,500 grams (Marsubrin, Rohsiswatmo, & Sjarif, 2021).

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Preterm labour is a problem experienced by every country in the world. According to WHO, there are around 10-11% of preterm labour in the world every year. At the same time, in Indonesia itself, the WHO explains that there are around 16% of preterm labour, which places Indonesia ranked fifth with the largest preterm labour in the world (Maharani, 2021). The prevalence of preterm labour in Indonesia was 14 per 1,000 live births in 2016, 13.8 per 1,000 live births in 2017, and 29.5 per 1,000 live births in 2018 (Dimiyati, Fauzy, Chabib, Rafif, & Putra, 2020).

The main signs or symptoms of the presence of preterm labour itself are contractions in the uterus; the use of tocolytic therapy can inhibit uterine contractions aimed at prolonging gestational life and delaying labour. Given the advantages, giving Nifedipine can reduce blood pressure for 24 hours and Through / Peak ratio (T/P ratio) (Sudarwanto, 2017). The side effects of Nifedipine were relatively small; from studies that have been done, 35 people who get Nifedipine therapy, only 4 people experience weakness after therapy. (Hamzah, Manggau, & Nasruddin, 2017).

Does this study aim to determine whether tocolytic drugs are effective for management in pregnant women with the threat of parts premature imminent at PKU Muhammadiyah Gamping Hospital Yogyakarta.

## 2. Materials and Methods

In this study, the method used was analytical descriptive observational with a cross-sectional approach. This observation was carried out by taking medical record data at PKU Muhammadiyah Gamping Hospital Yogyakarta within the past 5 years.

The research sample taken was data on 53 pregnant women who experienced preterm labour at PKU Muhammadiyah Gamping Hospital Yogyakarta and received tocolytic therapy.

The sampling process is carried out non-randomly (nonprobability sampling) with the quota sampling technique by determining certain inclusion and exclusion criteria with a predetermined amount.

Inclusion criteria include:

1. Pregnant women aged 20 – 40 years.
2. Pregnant women with gestational age trimester II and trimester III.
3. Getting tocolytic therapy.
4. Pregnant women who are diagnosed with Partus Prematurus Imminens (PPI).

Exclusionary criteria, including:

1. Have a history of surgery.
2. Pregnant women with severe preeclampsia/eclampsia.
3. Have a history of heart disease.
4. Have a history of hypotension.
5. Have a history of anaemia.

## 3. Results and Discussions

Based on the results of research that has been conducted on 24 samples:

**Table 1**  
**Characteristics of Age Samples of Pregnant Women at PKU Muhammadiyah Gamping Hospital Yogyakarta**

Sample Characteristics		
Age of Pregnant Women (th)	Frequency (n)	Percentage (%)
Reproductive (20-35 years)	22	91,7
Risk (< 20 and > 35 years)	2	8,3

Sum	24	100
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Table 1 shows that this study's samples were mostly of people of reproductive age (20-35 years), as many as 22 (91.7%) people.

**Table 2**  
**Gestational Age of Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

No	Gestational Age	Frequency (n)	Percentage (%)
1	Trimester 2 (14-28 mg)	2	8,3
2	Trimester 3 (28-40 mg)	22	91,7
Total		24	100

Table 2 shows that most samples with gestational age in the 3rd trimester (28-40 mg) are 22 (91.7%) people.

**Table 3**  
**Use of Drugs in Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

No	Drug Use	Frequency (n)	Percentage (%)
1	Nifedipine	13	54,2
2	Isoxuprine	11	45,8
Total		24	100

Based on Table 3, it is known that most samples used Nifedipine drugs, as many as 13 (54.2%) people.

**Table 4.**  
**Effectiveness of Drugs Given to Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

No	Effectiveness	Frequency (n)	Percentage (%)
1	Succeed	23	95,8
2	Unsuccessful (Moved RS)	1	4,2
Total		24	100

Based on Table 4, it is known that most of the sample succeeded as many as 23 (95.8%) people.

**Table 5**  
**Relationship between Age Sample Characteristics of Pregnant Women with Drug Use in Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

Age of Pregnant Women	Drug Use		Total n (%)	$X^2$ (p-value)
	Nifedipine n (%)	Isoxuprine n (%)		

Reproductive (20-35 years)	12	10	22	
At risk (< 20 and > 35 years)	1	1	2	0,015 (0,717)
Total	13	11	24	

Based on Table 5, it is known that most pregnant women are of reproductive age (20-35 years) with the use of Nifedipine drugs as many as 12 (50%) samples (Jesica & Friadi, 2019). The Fisher Exact Test obtained a value = 0.717 where  $p > 0.05$ . This means that there is no significant relationship between the age characteristics of pregnant women and the use of drugs in pregnant women with premature parts imminent.

**Table 6**

**The Relationship between Gestational Age and Drug Use in Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

Gestational Age	Drug Use		Total n (%)	$\chi^2$ (p-value)
	Nifedipine n (%)	Isoxuprine n (%)		
Trimester 2	2	0	2	
Trimester 3	11	11	22	1,846 (0,283)
Total	13	11	24	

Based on Table 6, it is known that the most gestational age in Trimester 3 with the use of Nifedipine drugs as many as 11 (45.8%) samples. The Fisher Exact Test obtained a value = 0.283 where  $p > 0.05$ . This means that there is no significant relationship between gestational age and drug use in pregnant women with premature parts imminent.

**Table 7**

**The Relationship between Gestational Age and Drug Effectiveness in Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

Gestational Age	Effectiveness		Total n (%)	$\chi^2$ (p-value)
	Succeeded n (%)	It didn't work n (%)		
Trimester 2	2	0	2	
Trimester 3	21	1	22	0,095 (0,917)
Total	23	1	24	

Table 7 shows that most of the gestational age in the 3rd trimester with cured status recovered as many as 21 (87.5%) samples. The Fisher Exact Test obtained a value = 0.917 where  $p > 0.05$ . This means that there is no significant relationship between gestational age and cure in pregnant women with premature parts imminent.

**Table 8**  
**Relationship between Drug Use and Drug Effectiveness in Pregnant Women with Partus Prematurus Imminens at PKU Muhammadiyah Gamping Hospital Yogyakarta**

Drug Use	Effectiveness		Total n (%)	X <sup>2</sup> (p-value)
	Succeeded n (%)	It didn't work n (%)		
Nifedipine	12	1	13	0,883 (0,542)
Isoxuprine	11	0	11	
Total	23	1	24	

Based on Table 8, it is known that the most use of Nifedipine drugs with cured status was 12 (50.0%) samples. The Fisher Exact Test obtained a value = 0.542 where  $p > 0.05$ . This means that there is no significant relationship between drug use and cure in pregnant women with premature parts imminent (Widiana, Putra, Budiana, & Manuaba, 2019).

### Sample Characteristics

Pregnant women with the threat of preterm labour or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta for 5 years (2016 – 2021) were found to have as many as 53 people as research subjects. The patient's medical records found with data were quite complete, as many as 24, so only 24 subjects could be taken for this study. Twenty-four subjects were studied, and most pregnant women were classified as productive age group (20-35 years), namely as many as 22 people (91.7%). This shows that in terms of age, pregnant women at PKU Muhammadiyah Gamping Hospital Yogyakarta, the research subjects, are the productive age group. High-risk pregnancies are pregnancies that can cause pregnant women and babies to become ill and die before delivery takes place (Nuryanti, 2021). Babies die or are disabled, and even mothers die during childbirth, often in pregnancies aged 35 years and over. There are many risk factors for pregnant women, and one of the important factors is age. Pregnant women at the age of more than 35 years are at higher risk of getting pregnant than when pregnant at a normal age, which usually occurs around 21-30 years. Aged 35 years and over, babies born are susceptible to genetic disorders. At reproductive age (25-35 years), the risk of babies experiencing genetic disorders is 1:1000, while in mothers over 35 years old, the risk increases to 1:4. Therefore, the age of the mother for childbirth should be in the range of 25-35 years (Shibuya et al., 2013). In addition, a person's age can also affect a person's information and experience, which this study is about the use of tocolytic therapy in pregnant women with premature parts imminent. Someone who gets more information will add broader knowledge, while experience, which is something someone has done, will increase knowledge about something informal (Maharani, 2021).

### Incidence of Preterm Labor

The incidence of preterm labour or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta, which was recorded for 5 years (2016 – 2021), was 55 people. Partus Prematurus Imminens (PPI) or preterm labour is a threat of labour that occurs in the third trimester (28-40 weeks). This arises due to uterine contractions at <37 weeks gestation caused by many factors from the mother. The main signs or symptoms of the presence of preterm labour itself are contractions in the uterus; the use of tocolytic therapy can inhibit uterine contractions aimed at prolonging gestational life and delaying labour. Another problem that can occur during preterm labour lies in the baby; babies born prematurely will have a higher risk of death compared to babies born normally (Zulaikha & Minata, 2021). Preterm labour is dangerous because it has the potential to increase perinatal mortality by 60-80%; usually, preterm labour is associated with low birth weight (BBLR). Low birth weight (BBLR) is caused by premature birth and stunted fetal growth (POGI, 2011; Clinical Practice Guideline, 2015). Some risk factors that play a role in parts premature imminent include multiple pregnancies, polyhydramnios, uterine anomalies, cervical dilation at 32 weeks gestation, history of abortion 2 or more times in the second trimester, history of previous preterm labour, history of undergoing surgical procedures on the cervix, cervical flattening/shortening of less than 1 cm in 32 weeks of pregnancy, and abdominal surgery after the first trimester (Andalas et al., 2018).

### The effectiveness of tocolytic therapy

Twenty-three (95.8%) pregnant women with Partus Prematurus Imminens were hospitalised and recovered. This shows that effective tocolytic therapy given to pregnant women with preterm labour or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta is effective. The results of this study are supported by Refisari (2020) and Yasa et al. (2019), where the results showed that effective tocolytic therapy was given to pregnant women with preterm labour. Tocolytic is a pharmacological agent given to prevent premature birth; this agent will relax the uterine myometrium and inhibit uterine contractions to prolong pregnancy and reduce neonatal complications. Tocolytic therapy is contraindicated if the prolongation of gestational age may cause harm or harm to the mother or fetus. Contraindications of tocolytic therapy itself include antepartum haemorrhage, chorioamnionitis, advanced cervical dilatation, placental insufficiency, abnormal CTG, lethal congenital/chromosomal malformation, preeclampsia/eclampsia, maternal allergy to tocolytics (Simhan, 2017).

#### **Tocolytic Therapy Class**

The drug given to pregnant women with Partus Prematurus Imminens is Nifedipine for as many as 13 (54.2%) people, while others get Isoxuprine. This shows that the group of tocolytic therapy that is widely given to pregnant women with preterm labour or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta is Nifedipine. The results of this study are supported by (Suff, Story, & Shennan, 2019), who showed that Nifedipine is the group of tocolytic therapy widely given to pregnant women with preterm labour. There are many classes of tocolytic drugs other than magnesium sulfate (MgSO<sub>4</sub>), such as Calcium Channel Blockers, betamimetics, and NSAIDs. The most widely used tocolytic drug class in Indonesia is the Calcium Channel Blocker class, such as Nifedipine. According to the Food and Drug Administration (FDA), Nifedipine is included in category C in the drug safety category. However, in Indonesia itself, research on the success rate of Nifedipine drugs as a tocolytic therapy to prevent preterm labour is still rarely done. Nifedipine administration can reduce blood pressure for 24 hours and Through / Peak ratio (T/P ratio) (Sudarwanto, 2017). Side effects of Nifedipine are relatively small; from studies that have been conducted, 35 people who get Nifedipine therapy, only 4 people experience weakness after therapy (Hamzah et al., 2017).

#### **Duration of drug administration**

The duration of drug administration recorded in medical records only existed in 7 research projects. The duration of tocolytic administration in the seven subjects was <2 x 24 hours. This is supported by (Prawiharjo, 2014), where a meta-analysis proves that tocolytic drugs can extend the latent phase of preterm labour for 2x24 hours or 24-48 hours.

## **4. Conclusion**

There were 23 subjects (95.8%) pregnant women with preterm labor or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta recovered by giving tocolytic therapy. There was no significant relationship between gestational age and the administration of Nifedipine and Isoxuprine drugs in the recovery of pregnant women with Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta.

Overall, there was no significant relationship between gestational age and drug use in pregnant women with parts prematurely imminent. There was no significant relationship between gestational age and drug use with cure in pregnant women with partus prematurus imminens or Partus Prematurus Imminens (PPI) at PKU Muhammadiyah Gamping Hospital Yogyakarta (p-value > Level of Significant = 0.05). The results of this study are supported by Refisari (2020) and Yasa et al. (2019), which showed that there was no relationship between gestational age and drug use with cure in pregnant women with premature infants.

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