



# Electrocardiographic Pattern of Pregnant Women with Advanced Maternal Age

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## ABSTRACT

**Background:** Advanced maternal age (AMA) is becoming increasingly common and is associated with increased maternal and fetal morbidity and mortality. Around 22,2% of maternal deaths were found to be from cardiovascular disease, and women with higher cardiovascular mortality were likely older. Electrocardiography (ECG) is a simple tool for detecting cardiovascular problems. Though there are many studies of the ECG in normal pregnant women, there is still limited data on the ECG pattern in pregnant women with AMA.

**Objective:** Describe the characteristics of the ECG pattern in woman with AMA.

**Methods:** This study used data retrospectively from medical records of patient in Kariadi General Hospital Semarang from 1st to 30th October 2018. The inclusion criteria were advanced age  $\geq$  35 years, in the last trimester. Demography, clinical, laboratory, and 12-lead ECG data were collected and reported.

**Results:** Thirteen patients were obtained, with mean age of 38,3 years. Majority of patients had preeclampsia (61,5%) and superimposed preeclampsia (15,4%). Mean systolic blood pressure was 168 mmHg. All of the patients was sinus rhythm, with a mean heart rate 92,5 bpm. Mean QTc was 430,7ms, with 3 patients (23,1%) having borderline prolongation grade. Another abnormality was a left atrial abnormality in 3 patients (23,1%), poor R wave progression in 2 patients (15,4%), and a pathological Q wave in 1 patients (7,7%).

**Conclusion:** ECG abnormalities are seen in 38,4% of pregnant women over 35 years old. The performance of an ECG in AMA may be a first step toward improved pregnancy outcomes since it is widely available and easily interpreted by general practitioners

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## 1. Introduction

Advanced maternal age (AMA) is defined as childbearing in a woman over 35 years of age, usually growing in high income countries.<sup>1</sup> In Canada and United States of America, births occurring among women of advanced maternal age account for approximately 8% and 11% of all first births, respectively.<sup>2</sup> In England and Wales, 20% of births were to women aged 35 years and over.<sup>3</sup> In Indonesia, Besari et al found that women with AMA would like to have premature rupture of the membranes (PROM) (23,3%), and preeclampsia (22,8%). The results of the logistic regression test showed that PROM was associated with the incidence of surgical delivery (OR 1.92, 95% CI 1.112-3.333). Meanwhile, placenta previa (OR 8.06 with 95% CI 2.681-24.238) and position abnormalities (OR 2.78 with 95% CI 1.532-

5.050) were related to length of hospitalization.<sup>4</sup> The changes in reproductive behavior due to socio-economic improvements, longer education, and difficulties associated with finding jobs. Therefore, women started becoming pregnant at a late age.<sup>1</sup>

AMA is associated with an increased risk of pregnancy complications leading to maternal and perinatal morbidity and mortality.<sup>1,5</sup> In a study investigating during pregnancy up until one year postpartum, 22.2% of maternal deaths were found to be from cardiovascular disease and women with cardiovascular mortality were likely older and die during postpartum.<sup>6</sup> The most frequent etiology was cardiomyopathy, while the arrhythmic deaths were the third most common cause.<sup>6</sup>

Electrocardiogram (ECG) is a simple tool for detecting cardiovascular problems, that universally available and feasible in developing countries. ECG is an important component and potential tool to identify

risk for the development cardiovascular problems which increased in woman with AMA.<sup>5,7</sup> Zhao et al, observe the late pregnancy women with AMA and found that patient with abnormal ECG easily suffer from pregnancy losing, premature birth and having a low birth weight baby.<sup>5</sup> Although there are many studies of the ECG in normal pregnant women, there is still limited data on the ECG pattern in pregnant women with AMA.

Our study aimed to describe the characteristics of the ECG pattern in women with AMA.

## 2. Methods

This descriptive study used data retrospectively from medical records of patient in Kariadi General Hospital Semarang from October 1st to 30th October 2018. All consecutive advanced age  $\geq$  35 years in the last trimester according to last menstrual period and ultrasonographic measurements. We collect demographic data such age and education level; the clinical data were weight, height, systolic and diastolic BP, and multi-parous or not. Later, the body mass index (BMI) was calculated from weight/height<sup>2</sup> (kg/m<sup>2</sup>). The laboratory data were hemoglobin, urea, and creatinine.

A 12 lead ECG was recorded for each woman in the 3rd semester at rest in the supine position. Recordings were acquired at a paper speed of 25mm/s, with 10 mm/mV standardization. The ECG was analyzed both qualitatively and quantitatively. ECG parameters such as rhythm, heart rate, P wave, QRS wave, T wave, U wave morphology, PR interval, QRS duration, QT interval, voltage, atrial and any abnormality were collected. Heart rate (HR) was calculated by dividing 1500 by the R to R interval in small squares. The electrical axis was determined using the Baltazar method.<sup>8</sup> PR interval was measured as the time between the beginning of the P wave and the beginning of the QRS complex in millisecond (ms). QRS duration was measured from the start until the end of QRS complex in ms. Sokolow-Lyon voltage was taken from the bigger summation between S wave in V1 and R wave in V5 or V6.<sup>9</sup> QT interval was measured as the time from the start of Q wave to the end of T wave and corrected by HR using Bazett's formula.<sup>10</sup> The criteria for left atrial abnormality were

(1) widely notched P wave (40 ms), (2) terminal negative component of the P wave in lead V1 with duration  $\geq$ 40 ms and amplitude  $\geq$  -0.1 mV, or (3) P wave duration  $\geq$ 120 ms.<sup>11</sup> The QTc prolongation grades for females were  $\leq$ 450ms (normal), 451 to 470 ms (borderline), and  $\geq$ 470 ms (prolonged).<sup>12</sup> Poor R wave progression was defined as R-wave amplitude  $\leq$  0.3 mV in lead V3 and R-wave amplitude inlead V2  $\leq$  R-wave amplitude in lead V3.<sup>13</sup>

Statistical analysis was performed using SPSS version 23. Data are reported in percentage, mean  $\pm$  standard deviation (SD), or median (minimum – maximum) according to the type of data.

## 3. Results

During the study duration, 13 samples were obtained. The baseline characteristics of the patients are shown in Table 1 . The average age distribution of the patients was  $38,3 \pm 2,7$  years. All the patients in this study were multiparous. As shown in table 1, mean gestational age of the patients was  $33,1 \pm 3,9$  weeks. There were 11 patients (84,6%) who has stage 2 hypertension, 1 (7,7%) pre-hypertension and 1 (7,7%) normal arterial pressure. Most of the patients were diagnosed with preeclampsia with 8 patients (61,5%), the rest had superimposed preeclampsia on 2 patients (15,4%) , gestational hypertension on 1 patients (7,7%) and chronic hypertension on 1 patients (7,7%). In the laboratory examination, the hemoglobin level was  $12,5 \pm 1,2$  g/dl, urea was  $15,7 \pm 5,2$  mg/dl, and creatinine was  $0,71 \pm 0,14$  mg/dl.

### ECG characteristics

These form the main result of the study. All of the patients was sinus rhythm, mean heart rate was  $92,5 \pm 11,0$ , there are five patients (38,4%) who have tachycardia. All of the patient have normal cardiac axis ( $-30^\circ$  until  $+90^\circ$ ) with mean  $33,3 \pm 21,7^\circ$  . There was normal PR interval and QRS duration with median 160,0 (120,0-200,0) ms, and 80,0 (60,0-80,0)ms respectively. Mean QTc by Bazett formula was  $430,7 \pm 26,3$ , with 3 patients (23,1%) have borderline prolongation grade. Another abnormality on the ECG was left atrial abnormality in 3 patients (23,1%), poor R wave progression in 2 patients (15,4%), and a pathological Q wave in 1 patients (7,7%).

**Table 1.** Subject Characteristics

Parameters	All n=13
<b>Demography</b>	
Age, years	38,3 ± 2,7
Gestational age, weeks	33,1 ± 3,9
Weight, kg	76,5 ± 12,9
Height, cm	154,1 ± 6,2
Body mass index, kg/m <sup>2</sup>	32,2 ± 5,0
<b>Clinical</b>	
Systolic blood pressure, mmHg	168,0 ± 26,9
Diastolic blood pressure, mmHg	101,6 ± 16,1
Hypertension status n, (%)	
Normal	1 (7,7)
Pre-hypertension	1 (7,7)
Stage 1 Hypertension	0
Stage 2 Hypertension	11 (84,6)
Multiparous, n (%)	13 (100)
Diagnosis, n (%)	
Pre-eclampsia	8 (61,5)
Superimposed pre-eclampsia	2 (15,4)
Gestational Hypertension	1 (7,7)
Chronic Hypertension	1 (7,7)
<b>Laboratory</b>	
Hemoglobin, g/dL	12,5 ± 1,2
Ureum, mg/dL	15,7 ± 5,2
Creatinine, mg/dL	0,71 ± 0,14
<b>Electrocardiography</b>	
Sinus rhythm, n (%)	13 (100%)
Heart rate, beats per minute	92,5 ± 11,0
Axis, degree	33,3 ± 21,7
Normal Axis, n (%)	13 (100)
PR interval, ms	160,0 (120,0-200,0)
QRS complex duration, ms	80,0 (60,0-80,0)
Sokolow-Lyon voltage, mV	1,41 ± 1,68
Left Ventricular Hypertrophy, n(%)	0
Corrected QT interval, ms	430,7 ± 26,3
QTc prolongation grade	
Normal	10 (76,9)
Borderline	3(23,1)
Abnormal/Prolonged	0
Left atrial abnormality, n (%)	3 (23,1)
Poor R Wave Progression, n (%)	2 (15,4)
Pathological Q wave, n (%)	1 (7,7)

Values are shown as mean ± standard deviation, median (minimum – maximum ) or percentage

This retrospective study showed that almost all of the patients with AMA were in the hypertension stage (84,6%), with the most patients in preeclampsia (61,5%) and superimposed preeclampsia (15,4%)

#### 4. Discussions

condition. This did not reflect all of the AMA patients since the ECG examination in our hospital was not a routine examination except for special or emerging conditions such as preeclampsia.

Our ECG finding in patient with AMA reported there are abnormality on corrected QT interval, left atrial abnormality, presence of poor R wave progression and pathological Q wave. Zhao et al who observed the change of the electrocardiogram on older pregnant women ( $\geq 35$  years) reported that the incidence of abnormal ECG was found to be higher in the older pregnant group, with ST segment changes and different types of arrhythmia, such as sinus bradycardia and ventricular premature beat being more common in that group.<sup>5</sup> The outcome of the study also showed that patients with AMA and an abnormal ECG suffered more pregnancy loss, premature birth, and low birth weight significantly.<sup>5</sup> Even though there are different ECG characteristics from the recent study, we found one patient with a pathological Q wave that may represent an ischemic condition just like ST segment changes.

We found 3 patients (23,1%) have a left atrial abnormality, and 3 patients (23,1%) have a borderline stage of prolonged QTc. Aslan et al also found the maximum QTc, minimum QTc, and QTc dispersion were significantly higher in advanced age pregnancies compared to the control group (<35 years old). In the correlation analysis, the increased dispersion of QTc and P were positively correlated with maternal age.<sup>7</sup> Recently, Braschi et al. demonstrated the increase in

ventricular repolarization markers with increased age.<sup>14</sup> Hypertension, which we found most prevalent in our patient also has a contribution, present evidence demonstrated that hypertensive disorders of pregnancy were associated with changes of the P wave morphology and QT interval. Raffaelli et al analyzed ECG in hypertensive pregnant women and found that significant changes in QT, QTc and QTd intervals along with changes in ventricular repolarization were observed among hypertensive women.<sup>15</sup> Inci et al also studied ECG among pre-eclamptics and demonstrated that the duration of atrial electromechanical delay and P wave dispersion (Pd) was more prolonged in hypertensive pregnant women.<sup>16</sup> Angeli et al reported that left atrial abnormality diagnosed by P wave changes in lead V1 is an independent predictor of hypertensive disorder during pregnancy.<sup>17</sup> Another study shows that ECG abnormalities are seen in 14,2% of preeclamptic women.<sup>18</sup>

Zhao et al attempted to use ECG changes as a predictor for pregnancy outcomes in older pregnant women. In their study, it was determined that women older than 35 with ECG changes had a much higher rate of fetal loss, prematurity, and low birth weight.<sup>5</sup>

This research had some limitations, including a small sample size, the usage of secondary retrospective data, the limitation of ECG examination in our hospital to patients with special conditions such as hypertension or pre-eclampsia, and the manual interpretation of ECG, which allows for inter- and intra-observer variability.

## ECG EXAMPLE

Figure 1. 41 years old women, 37 weeks of gestational age, history of hypertension and dyslipidemia. ECG showed sinus rhythm, 105 bpm, normoaxis, Poor r wave progression (red circle).

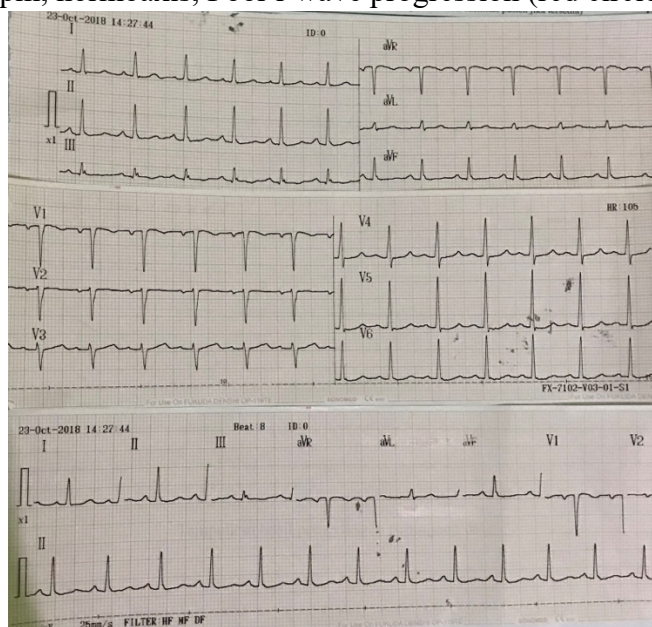
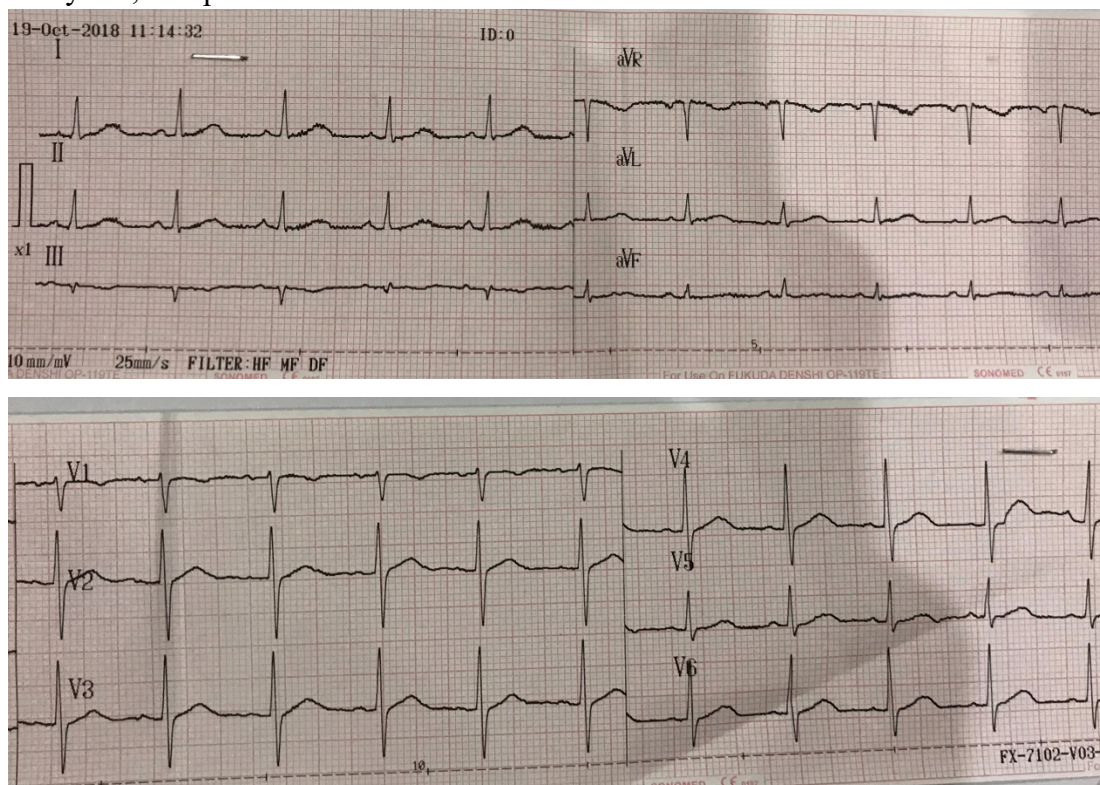


Figure 2. 44 years old women, 29 weeks of gestational age, history of hypertension. ECG showed normosinus rhythm, 90 bpm.



## 5. Conclusion

ECG changes such as a corrected QT interval, left atrial abnormality, presence of poor R wave progression, and a pathological Q wave were observed in pregnant women with advanced maternal age. Even though most of our patients have hypertension, there are studies that show that AMA women are likely to have ECG abnormalities such as myocardial ischemia, arrhythmia, and QTc prolongation, which have a much higher rate of fetal loss, prematurity, and low birth weight. Performance of an ECG in AMA may be a first step toward improving pregnancy outcomes and future cardiovascular health for patients. ECG is also widely available even in remote health centers and can be easily interpreted by a general practitioner. Thus, before recommending that every AMA undergo an ECG, further studies are required.

## Ethical Approval

Ethical recommendation by health research ethics committee faculty of Medicine Diponegoro University

## Conflicts of Interest

There is no conflict of interest in this research

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## Author Contributions

Arjaty Pramadita Mangkoesobroto : Conception and design, acquisition of data, analysis, drafting the article, revision of the article, final approval. Besari Adi Pramono : Conception and design, acquisition of data, revision of the article, final approval. Aruman Yudanto Ariwibowo Binarso Mochtar : Conception and design, revision of the article, final approval

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