Late Referral of Eisenmenger Syndrome in Pregnancy at Dr. Soetomo Hospital Surabaya

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ABSTRACT

Keywords: Eisenmenger, pregnancy, late referral

Background: Pregnancy with Eisenmenger syndrome is an obstetric problem which numbers keep rising every year. The cases require specific, decisive, and multidisciplinary approach. The unavailability of accurate diagnostic procedures, as well as the national consensus that has not been agreed on, all contributes to the increasing number of late referral that cause morbidity and the high risk of mortality. **Purpose:** To know number and cause of late referral cases with Eisenmenger syndrome at Dr. Soetomo General Hospital, Surabaya in 2018-2019. **Methods:** Retrospective study by using medical records data of Dr. Soetomo General Hospital, Surabaya on January 2018-December 2019. **Result:** There are 18 cases of Eisenmenger syndrome from January 2018 to December 2019. Approximately 3 cases are timely referral while 15 cases are late referral cases. From those 15 late referral cases, about 12 cases (80%) are pregnant. Based on the risk factors, 73% of the patients have a congenital heart disease (Atrial septal defect) and severe pulmonary hypertension. In the postpartum referral cases group, 3 cases were referred because of suspected heart disease postpartum. Nearly all of the late referred cases have a bad prognosis those maternal deaths. There were 7 maternal deaths caused by cardiogenic shock. Regarding the source of referral, the majority of referred pregnant patient comes from out of Surabaya (73%), while for the postpartum patient, 13% was referred from out of Surabaya. According to the referral types, the majority of the late referral cases are emergency referral (73%), as for the postpartum referral, 20% are emergency referral. **Conclusion:** The number of late referral in Eisenmenger syndrome in Dr. Soetomo general hospital is still high. Further socialization and trainings regarding the early detection and management of Eisenmenger syndrome is still very much needed.

Introduction

Congenital heart disease (CHD) is most common from of congenital abnormalities and is present in 0.8-0.9 % of all births (Regitz, 2018). In women with congenital heart disease pregnancy is generally well tolerated, but in contrast in up to 10% of complicated pregnancies maternal cardiac complications (Conobbio, 2017). Eisenmenger syndrome is very rare in
pregnant women with an incidence of about 3% in the pregnant patients with congenital heart defects (Rathod, 2014). Eisenmenger syndrome is known as pulmonary hypertension due to high pulmonary vascular resistance with bidirectional shunt at aortopulmonary, ventricular or atrial level. Eisenmenger patient require special consideration because of the additional complications of cyanosis, right to left shunt and paradoxical embolism. During pregnancy systemic vasodilatation increase the right to left shunt and decrease pulmonary flow, leading to increase cyanosis and a low cardiac output. Maternal mortality is high and termination of pregnancy should be discussed (Duan, 2016).

The cases require specific, decisive, and multidisciplinary approach. The unavailability of accurate diagnostic procedures, as well as the national consensus that has not been agreed on, all contributes to the increasing number of late referral that cause morbidity and the high risk of mortality. Early detection in Eisenmenger pregnant woman become the most effective method for early detection, first treatment and referring to tertiary hospital. Proper history taking and physical examination will help reduce late referral (Pieper, 2011). Mortality due to Eisenmenger syndrome can be prevented if referred at the right time to tertiary hospital. In this study we will analyze late referral during pregnancy and post partum with Eisenmenger syndrome who have been treated at Soetomo Hospital since 2018-2019. This is very important so that obstetricians, medical doctor or midwife are more aware and provide planned early referral to be handled by the multidisciplinary tim in tertiary hospital.

Method

This study was a retrospective study using electronic medical data records in Dr. Soetomo general hospital at January 2018 until December 2019. The inclusion criteria of this study were pregnant woman and post partum with late referral Eisenmenger syndrome, while for exclusion criteria were woman with time referral Eisenmenger and heart disease with pregnancy without Eisenmenger syndrome. From these data we traced the number and cause of late referral Eisenmenger in pregnancy and post partum.

Result and discussion

This study is retrospective using secondary data from medical records in Dr. Soetomo hospital Surabaya during 2018-2019. Inclusion criteria for this study is late referral cases pregnant woman and post partum with Eisenmenger syndrome that hospitalization at Dr. Soetomo hospital. Demographic data we analyze from age, parity, gestational age, kind of congenital heart disease, kind of referral, antenatal care, and mortality cases. The data we followed since the patient diagnosed Eisenmenger syndrome until we terminate this patient and the patient discharged from hospital or passed away. There are 18 cases of Eisenmenger syndrome from January 2018 to December 2019. Approximately 3 cases are timely referral while 15 cases late referral. During 2019 there was an increase in cases of pregnancy with Eisenmenger syndrome which is a maternal death as in the diagram below.
Pregnancy in patients with Eisenmenger syndrome is associated with significant maternal and fetal morbidity and mortality. Maternal mortality with Eisenmenger syndrome ranges from 30-70% (Karelkina, 2019). Because of the high risk of maternal mortality, pregnancy is contraindicated in women with Eisenmenger syndrome and usually spontaneous abortion occurs. Decreased oxygenation causes impaired fetal growth (Cunningham, 2014). The reported rate of maternal mortality in Eisenmenger syndrome has ranged from 20-50%, however even termination of the pregnancy is accompanied with adverse event. The preconception counselling and contraception in these patients is paramount importance (Galie, 2016).

Picture 2 and 3 shows that there are 18 cases of Eisenmenger syndrome from January 2018 to December 2019. Approximately 3 cases are timely referral while 15 cases are late referral cases. From those 15 late referral cases, about 12 cases (80%) are pregnant. The patients with timely referral are the patients who referred at the first and second trimester (< 20 wga and 20-27 wga) of pregnancy.
surabaya. And the type of referral, 11 pregnant and 3 post partum patients with emergency referral, and 1 patient with policlinic referral. This condition shows that early detection heart disease in pregnancy and late referral dominated by medical facility outside surabaya. Management of Eisenmenger syndrome outside surabaya still not yet optimal so late ini detecting and referring. Further guidance regarding heart disease in pregnancy especially Eisenmenger syndrome with the aim of finding out the accuracy of the diagnosis or screening of obstetrician and cardiologist must still be routinely done (Warnes, 2019).

Researchers found that patients with late referral were dominated by congenital heart disease atrial septal defect (ASD) as 11 cases (73%), Ventricle septal defect (VSD) 3 cases (20%) and Patent Ductus Arteriosus (PDA) 1 case (7%).

**Picture 6.** Distribution of congenital heart disease

The development of Eisenmenger syndrome may accompany a variety of forms of Congenital Heart disease. In one study 201 patients the most common defects were ventricular septal defects (33 percent), atrial septal defect (30 percent) and patent ductus arteriosus (14 percent). Other disorders including complex anatomic abnormalities can also be associated with Eisenmenger syndrome. In all cases, a communication between the systemic and pulmonary circulations is present. In some conditions, the normal anatomic relations between the atria, ventricles and great vessels may be altered (Stout, 2018).

Physical examination of patient with Eisenmenger syndrome demonstrates central cyanosis and digital clubbing. Most affected patients have diffuse central cyanosis, and clubbing involves all extremities equally. (Stout 2018)

In this study there were 15 cases late referral of pregnancy and post-partum with Eisenmenger syndrome. A total 10 received antenatal care in midwife, 4 patients by obstetrician and only one patient get antenatal care from obstetrician and cardiologist. It is not in accordance with the recommendation of European Society of Cardiology (ESC) that all pregnancies with heart disease should receive in hospital with maternal risk based group. Adequate antenatal care in regional hospitals and evaluation of heart conditions will reduce late referral and decrease maternal mortality (Warnes, 2019).

**Picture 7.** Distribution of antenatal care

**Picture 8.** Distribution numbers of antenatal care
Indonesia were using integrated antenatal care system with 4 visits during pregnancy, namely 1 time in first trimester, one time in second trimester and 2 times in third trimester. To achieve a more optimal pregnancy outcome, WHO in 2016 issued recommendations on antenatal care. The recommended number of antenatal care is 8 visits. Recommended antenatal visit are not only in quantity, but also quality with early detection efforts, monitoring maternal and infant health status and providing interventions according to existing problem. Inadequate antenatal visits (less than 8 visits at term pregnancy) increased the risk of maternal death by 1.7 times (WHO, 2016).

Picture 8 shows in this study the number of inadequate antenatal visits (less than WHO recommendation)) around 80% patients. The delay to detecting a heart disease where a new heart disease is discovered after pregnancy increased the mortality risk of 2.5 fold compared to when a heart disease is detected before pregnancy (James, 2019). This is consistent with previous research that the risk of pregnancy should have been diagnosed before pregnancy so that management during pregnancy and childbirth can be prepared.

Pregnancy in patients with Eisenmenger syndrome is associated with significant maternal and fetal morbidity and mortality. Because of the high risk of maternal mortality, pregnancy is contraindicated in women with Eisenmenger syndrome (Warne, 2019). Pregnant woman with Eisenmenger syndrome also have neonatal complications and preterm birth. Pregnant woman with heart disease have 6 times risk of having a premature baby born (Siu, 2010).

The majority of maternal deaths occur during or in the first week after delivery but can occur during gestation, labor, or more than one week after delivery (Scott, 2019). The fixed pulmonary arterial resistance cannot accommodate to the hemodynamic fluctuations of labor, delivery and the puerperium. Most deaths are due to thromboembolism, volume depletion, which can augment to the right to left shunt and precipitate intense cyanosis, and preeclampsia (Scott, 2019). In addition, a sudden increase in systemic vascular resistance may fatally reduce cerebral blood flow.

During January 2018 - December 2019 we found 7 cases maternal death from 15 late referral cases Eisenmenger syndrome (47%). From 7 cases referred at third trimester 3 and passed away after delivery at Dr. Soetomo hospital. The fastest death is 16 hours after caesarean section and the latest 10 days after caesarean section. This is the most dangerous time and causes the highest mortality in one to two weeks after delivery (Stout, 2018). As for the analysis of maternal death due to late referral:

**Table 1.** Analyze maternal death cause of late referral

| Characteristics                          | N (7) |
|------------------------------------------|-------|
| **Gravida**                              |       |
| Primigravida                             | 3     |
| **Risk Factors**                         |       |
| ASD + Severe pulmonal hypertension       | 6     |
| **Week gestational age**                 |       |
| < 37 wga                                 | 6     |
| ≥ 37 wga                                 | 1     |
| **Mode of delivery**                     |       |
| C-Section                                | 6     |
| Vaginal delivery                         | 1     |
| **Kind of referral**                     |       |
| Referral in Surabaya                     | 1     |
| Referral outside Surabaya                | 6     |
| Emergency referral                       | 6     |
| Obstetric outpatient clinic              | 1     |
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| Antenatal care |   |
|----------------|---|
| Midwife        | 5 |
| Obgyn          | 2 |
| Numbers of Antenatal care |   |
| < 8x (WHO recommendation) | 7 |
| ≥8x (WHO recommendation) | - |
| Cause of death |   |
| Cardiogenic shock | 7 |

Cardiogenic shock is the cause of maternal death Eisenmenger syndrome patients at Dr.Soetomo hospital during 2018-2019. In our study the fastest death was 16 hours after delivery and the longest 10 days after delivery. This way similar with research conducted by Shinji Katsurahgi in Japan that hemodynamic patients with Eisenmenger become unstable 24 – 72 hours after caesarean section and the highest sudden death caused by late diagnosis and hospitalization. (Katsurahgi 2012). The danger of maternal death can occur during pregnancy, especially advanced pregnancy, childbirth and early postpartum (Brennan, 2018). Research in UK has a poor prognosis in pregnant patients with Eisenmenger syndrome unless hospitalization during pregnancy, mortality remains high at around 40%. Most deaths occur at 7 until 35 days postdelivery. Late diagnosis and hospitalization increasing maternal mortality. Late diagnosis and hospitalization significantly increases maternal mortality (Easterling, 2012).

From our death case we have 6 patients terminate by c-section and 1 patient by vaginal delivery. With few exceptions, vaginal delivery is preferred over caesarean section as it carries lower risk for both mother and fetus due to smaller shifts in blood volume less haemorrhage, fewer clotting complications and fewer infections (Regitz, 2018). In our cases in third trimester almost all were delivered by C-section because of obstetric indication and the greater stability of hemodynamics, C-section may be safer than vaginal delivery for these patients with severe baseline hemodynamic abnormalities.

Late referral cases which is emergency referral is obtained 11 patients (73%) referred to while pregnant and post partum 3 cases (16%). And obstetric outpatient clinic is obtained 1 patient (7%) referred to while pregnant. 7 patients have inadequate antenatal care (less then WHO recommendation) that influence the risk of maternal mortality (WHO, 2016). Socialization of screening and timely polyclinic referral should be improved so that proper management can be carried out in antenatal preparation, pregnancy cases and post partum. Multidisciplinary therapy performed at a tertiary center by experienced obstetricians, anesthesiologist, neonatologist, and cardiologist are necessary to select the best treatment plan to optimize maternal and neonatal prognosis (Ashrai, 2017).

**Conclusion**

During 2018-2019 period at Dr. Soetomo hospital it was obtained 15 late referral cases who was referred while pregnant and post partum. Late referral 12 cases in pregnancy and 3 cases post partum, with maternal outcomes as many as 8 live patients and 7 patients died. From 7 cases maternal death is late referral with third trimester of pregnancy which died after delivery. In this study the cause of late referral might be related to maternal mortality was carried out. Inadequate antenatal visit and late detection can affects late referral and causes high mortality rates of patients with Eisenmenger syndrome.
Reference

Ashrafi, R., & Curtis, S. L. (2017). Heart Disease and Pregnancy. *Cardiology and Therapy*, 6(2), 157–173. https://doi.org/10.1007/s40119-017-0096-4

Brennan K, Hatch D. 2018. Eisenmenger syndrome. In Consult in Obstetric Anesthesiology (pp.185-187). Switzerland : Springer Nature

Cunningham F, Leveno G,Bloom KJ, Spong L, Dashe J, Sheffield JS. 2014.Congenital heart disease. In William Obstetrics (24th edition,pp. 973-999).USA:Mc Graw Hill.

Conobbio MM, Warnes CA,Aboulhosn J.2017. Management of pregnancy with complex congenital heart disease: a scientific statement for healthcare professional from the American Heart Association. 135:e50-87

Duan R, Xu X, Wang X, Yu H, You Y, Liu X, Xing A, Zhou R, Xi M. 2016. Pregnancy outcome in women with Eisenmenger’s syndrome: A case series from west China. BMC Pregnancy Childbirth ; 16 : 356 W.,

Easterling T, Stout K. 2012. Heart Disease. Obstetric Normal and Problem Pregnancies 6th ed. Philadelphia, Elsevier-Saunders; 36:825-850

Galie N, Humbert M, Vachiery JL. 2015. ESC Guidelines for the diagnosis and treatment of pulmonary hypertension: The Join Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology.Eur Heart J;37:67-119

James, P. R. (2019). *The importance of pre-pregnancy counselling in cardiac disease.* 1–17. https://doi.org/10.5837/bjc.2014.004

Karelkina E, Irtiyuga O, Kokonina Y, Yakubov A, Li O, Mazurok V, Moiseeva O. 2019. The pregnancy outcomes and delivery in women with Eisenmenger’s syndrome,

Katsurahgi S, Kamiya C, Tamanaka K, neki R, Iwanaga N, Miyoshi T, Horiuchi C. 2019. *Maternal outcome in pregnancy complicated with Eisenmenger syndrome.* 1–5.

Pieper. 2011. Pre- pregnancy Risk Assessement and Counselling of The Cardiac patient. Neth Heart journal, Volume 19, pp: 477-481

Rathod S, Samal SK. 2014. Successful pregnancy outcome in a case of Eisenmenger syndrome: a rare report. J Clin Diag Res. 8(10):0D08-9.

Regitz-Zagrosek V,Roos-Hesselink JW, Bauersachs J. 2018. ESC Guidelines for the managemet of cardiovascular disease during pregnancy. Eur Heart J.39;3165-241

Scott, N. S. (2019). *Management Of Cardiovascular Disease During Pregnancy.*1–6

Siu SC.,Balint OH, Mason J. 2010. Cardiac outcomes after pregnancy in woman with congenital heart disease. *Heart*: 96: 1656 - 1661

Stout KK, Daniels C.J, Aboulhosn JA. 2018 .AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease : A Report of the American College of cardiology/American Heart Association Task Force on Clinical Practice Guidelines J Am Coll Cardiol; 73:e81

Warnes, CA. 2019. *Pregnancy and Delivery in Women With Congenital Heart Disease Preconception Counseling.* 1–14

WHO. 2016. Guidelines Approved by the Guidelines Review Committee: WHO recommendations on antenatal care for a positive pregnancy,Geneva:World Heath Organization.