ORIGINAL ARTICLE

The correlation of nutritional status with hematology toxicity of adjuvant chemotherapy in ovarian cancer

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ABSTRACT

Objectives: To observe correlation of nutritional status using Nutritional Risk Index with the side effects of adjunctive haematological chemotherapy.
Materials and Methods: This study was a retrospective cohort study observing whether or not hematologic side effects occurred during chemotherapy based on medical records of postoperative ovarian cancer patients receiving adjuvant chemotherapy.
Results: Sixty-eight subjects with age range of 31-50 years (44.1%) multipara (68.8%), and advanced stage (52.1%) were observed. An increase was found in the diagnosis of malnutrition between the IMT method and NRI, which was 18.7% compared to 43.7%. A significant correlation was found between preoperative malnutrition and the incidence of anaemia after adjuvant chemotherapy for ovarian cancer patients (p=0.002). Whereas, in the event of leukopenia and thrombocytopenia, there were no significant correlations with p=0.675 and p=0.415, respectively.
Conclusion: There was an increase in malnutrition rate with the use of NRI compared with BMI and there was a significant correlation between malnutrition and side effects of anaemia in patients with ovarian cancer who underwent surgery and continued with adjuvant chemotherapy.

Keywords: ovarian cancer; nutritional status; adjuvant chemotherapy; maternal health

ABSTRAK

Tujuan: Mengetahui hubungan status nutrisi menggunakan Nutritional Risk Index dengan efek samping hematologi kemoterapi ajuvan.
Bahan dan Metode: Penelitian ini merupakan suatu studi kohort retrospektif yang mendata terjadi atau tidaknya efek samping hematologi selama kemoterapi berdasarkan data rekam medis penderita kanker ovarium pasca operasi yang mendapat kemoterapi ajuvan.
Hasil: Didapatkan 68 subyek dengan rentang usia terbanyak 31-50 tahun (44,1%) multipara (68,8%), dan stadium lanjut (52,1%). Didapatkan peningkatan diagnosis malnutrisi antara metode IMT dengan NRI, yaitu 18,7% dibandingkan 43,7%. Didapatkan hubungan yang bermakna antara malnutrisi pra operasi dengan kejadian anemia pasca kemoterapi ajuvan pasien kanker ovarium (p=0,002). Sedangkan pada kejadian leukopenia dan trombositopenia tidak didapatkan hubungan yang bermakna p= 0,675 dan p=0,415.
Simpulan: Didapatkan peningkatan angka malnutrisi dengan penggunaan NRI dibandingkan dengan IMT dan hubungan yang bermakna antara malnutrisi dengan efek samping anemia pada penderita kanker ovarium yang menjalani operasi dan dilanjutkan dengan ajuvan kemoterapi.

Kata kunci: kanker ovarium; status nutrisi; kemoterapi ajuvan; kesehatan ibu

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INTRODUCTION

Maternal Mortality Rate (MMR) and Infant Mortality Rate (IMR) are indicators of health development in the 2015-2019 National Mid-Term Development Plan and the SDGs. According to the Indonesian Health Data Survey, the Maternal Mortality Rate has decreased in the period 1994-2012, namely in 1994 of 390 per 100,000 live births, in 1997 it was 334 per 100,000 live births, in 2002 it was 307 per 100,000 live births, and in 2007 amounting to 228 per 100,000 live births. However, in 2012 the Maternal Mortality Rate increased again to 359 per 100,000 live births. In the IDHS 2012, the Infant Mortality Rate shows 32/1,000 live births (IDHS 2012), and in 2015, the 2015 Basic Health Research showed a decrease in MMR and IMR (MMR 305/100,000 live births; IMR 23/1000 live births). The highest cause of maternal mortality in 2016 was bleeding (32%) and 26% due to hypertension which causes seizures, and pregnancy poisoning so that the mother dies.[1]

Infant Mortality Rate is an indicator commonly used to determine the level of public health, both at provincial and national levels. IMR refers to the number of babies who die in the phase between birth and before reaching age 1 year per 1,000 live births. Currently, the Infant Mortality Rate (IMR) in Indonesia is the highest compared to other ASEAN countries. According to 2007 Indonesian Demographic and Health Survey (IDHS) data, the Infant Mortality Rate (IMR) in Indonesia is 34 per 1000 live births (Ministry of Health, 2009). According to the Ministry of Health of the Republic of Indonesia in 2008, one of the causes of newborn mortality is asphyxia (27%) which is the second cause of death for newborns after LBW. In 2009, the incidence of asphyxia in the world according to the World Health Organization (WHO) was 19%.[1]

This high maternal and infant mortality rate is due to the lack of health services in Indonesia. This is related to human resources (health workers), health infrastructure (health facilities), and the level of awareness of women of reproductive age in Indonesia regarding pregnancy planning and reproductive health. One of the factors associated with incorrect health services is the response time in diagnosing diseases of a pregnant woman and making decisions regarding the delivery process that will be taken. In general, the problems faced in meeting the response time are preparation for surgery (from informed consent to the operating room), anesthesia consultation, transportation of patients to the operating room, preparation for anesthesia, waiting time for the effectiveness of anesthetic action, the presence of operating personnel (obstetricians, anesthetists, pediatricians/neonatal officers, and surgical nurses) and the operation team cooperation.[2]

Decision to delivery interval (DDI) or response time is defined as the time interval in minutes from the time of cesarean section decision until the baby is born. The NICE RCOG (Royal College of Obstetrician and Gynecologist) Caesarean Section Guidelines states that the response time for category 1 cesarean section is 30 minutes and category 2 is between 30-75 minutes.[3]

In Indonesia, especially at Dr. Soetomo General Academic Hospital, Surabaya and at Universitas Airlangga Hospital Surabaya, Indonesia, there was no data on the response time of caesarea section in fetal distress patients. This study aimed to determine the response time of cesarean section in fetal distress patients in both hospitals in order to reduce infant mortality.

MATERIALS AND METHODS

This study was an observational analytic study with cross-sectional design using medical records at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital, Surabaya, Indonesia, in 2015-2017. The sample of this study was taken by total random sampling of all pregnant women with fetal distress who then underwent emergency cesarean section in 2015-2017. Furthermore, from these data the response time was calculated from the decision to operate until the birth of the baby based on the classification in Figure 1 in the process of delivery of fetal distress, which lasts 30 minutes.

RESULTS

Characteristics of the age of pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

From 2015-2017 pregnant women with fetal distress who underwent cesarean section at Dr. Soetomo General Academic Hospital, were as many as 103 patients with the characteristics of mostly aged >30 years (48 patients or 47% of all cases), then 20-30 years of age of 40 patients (38%) and the least were 15 patients (15%) aged of <20 years.

Characteristics of the age of pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

Between 2015-2017 pregnant women with fetal distress who underwent cesarean section at Universitas Airlangga Hospital, Surabaya were 5 patients with mostly 20-30 years of age (4 or 80% of all cases), then 1 case of age >30 years (20%) and there were no patients aged <20 years.

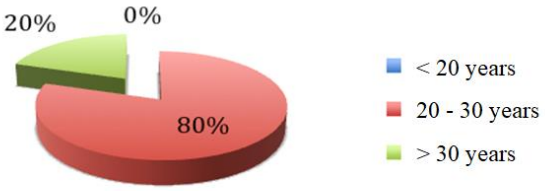

Figure 1. Age characteristics of pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

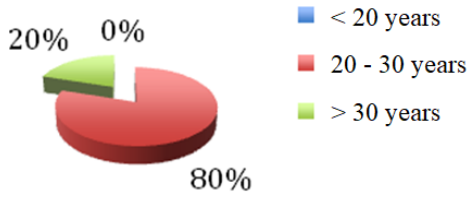

Figure 2. Age characteristics of pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

Characteristics of diseases of pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

These data indicate that the most fetal distress cases occurred in pregnant women with hypertension (68 cases/66%) and total placenta previa with bleeding in 4 cases (4%), and 7 cases of heart disease (7%).

Table 1. Disease characteristics of pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

No	Type of disease	Total
1	Hypertension	68
2	APB ec PPT	4
3	Heart disease	7
4	DM	2
5	Others	22
	Total	103

Characteristics of disease in pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

Three out of five cases of fetal distress pregnant women suffered from hypertension, whereas premature rupture of membranes was found in one case, and mal-presentation of vertex position in one case.

Table 2. Disease characteristics of pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

No	Type of disease	Total
1	Hypertension	3
2	PRM	1
3	Malpresentation	1
	Total	5

Selection of anesthesia for pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

Cesarean section procedure in pregnant women with fetal distress can be performed with two choices of anesthesia, the general anesthesia and regional anesthesia. This study found 63% of the cases underwent cesarean section using general anesthesia, while 37% used regional anesthesia.

Table 3. Selection of anesthesia for pregnant women with fetal distress undergoing cesarean section at Dr. Soetomo General Academic Hospital

No	Type of anesthesia	Total
1	General anesthesia	65 (63%)
2	Regional anesthesia	38 (37%)
	Total	103

Selection of the type of anesthesia for pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

Cesarean section in pregnant women with fetal distress can be performed with 2 choices of anesthesia, the general anesthesia and regional anesthesia. It was found that 80% of caesarean sections were performed with general anesthesia, while 20% used regional anesthesia.

Response time of pregnant women with fetal distress undergoing emergency cesarean section at Dr. Soetomo General Academic Hospital

This study found that the response time for the implementation of cesarean section in pregnant women with fetal distress mostly (83%) still needed >30

minutes, while the remaining 17% required <30 minutes.

Table 4. Selection of types of anesthesia for pregnant women with fetal distress undergoing cesarean section at Universitas Airlangga Hospital

No	Type of anesthesia	Total
1	General anesthesia	4 (80%)
2	Regional anesthesia	1 (20%)
	Total	5

Table 5. Response times of pregnant women with fetal distress undergoing emergency cesarean section at Dr. Soetomo General Academic Hospital

No	Response time	Total
1	< 30 minutes	18 (17%)
2	> 30 minutes	85 (83%)
	Total	103

Response time of pregnant women patients with fetal distress undergoing emergency cesarean section at Universitas Airlangga Hospital

This study found that the response time for the implementation of cesarean section in pregnant women with fetal distress was mostly (60%) more than >30 minutes, while the remaining 40% was performed <30 minutes.

Table 6. Response times of pregnant women with fetal distress undergoing emergency cesarean section at Universitas Airlangga Hospital

No	Response time	Total
1	< 30 minutes	2 (40%)
2	> 30 minutes	3 (60%)
	Total	5

Infant outcome from pregnant women with fetal distress at Dr. Soetomo General Academic Hospital

Most of infant outcomes from mothers with fetal distress who undergoing cesarean section at Dr. Soetomo General Academic Hospital was severe asphyxia with Apgar Score 1-3 in 58 cases (56.3%), moderate asphyxia in 37 cases (35.9%), and mild asphyxia in 10 cases (9.7%).

Table 7. Infant outcomes from cases of fetal distress at Dr. Soetomo General Academic Hospital

No	APGAR scores	Total
1	Mild asphyxia (7-10)	10 (9,7%)
2	Moderate asphyxia (4-6)	37 (35,9%)
3	Severe asphyxia (1-3)	58 (56,3%)
	Total	103

Table 8. Infant outcomes from cases of fetal distress in Dr. Universitas Airlangga Hospital.

No	APGAR scores	Total
1	Mild asphyxia (7-10)	0
2	Moderate asphyxia (4-6)	5
3	Severe asphyxia (1-3)	0
	Total	5

DISCUSSION

Characteristics of pregnant women with fetal distress undergoing cesarean section and infant output at Dr. Soetomo General Academic Hospital

In this study, at Dr. Soetomo General Academic Hospital we found that, from 103 patients, most of them were in the age range of >30 years, which were as many as 48 patients (47%), and the gestational age was mostly less than 37 weeks (premature), which was in 55 patients (53%). This was related to the underlying disease of the pregnant women, the hypertension, so that the delivery process did not wait for a full-term pregnancy. The babies were born at 34-37 weeks of gestation.[4]

As many as 66% of fetal distress cases occurred in mothers with hypertension and 12% in mothers with total placenta previa accompanied by bleeding. Apart from hypertension, total placenta previa, especially those with active flux, often results in fetal distress incidence. Hypertension is closely related to the incidence of chronic utero-placental flow insufficiency which may cause intrauterine fetal hypoxia, resulting in decreased fetal heart rate, leading to fetal emergency. In total placenta praevia totalis that is accompanied by bleeding, there is acute insufficiency of utero-placental flow which may lead to fetal distress.[4]

The most common type of anesthesia was general anesthesia which was performed in 65 patients (63%) compared to regional anesthesia in 38 patients (37%). Of the two types of anesthesia, general anesthesia is the main choice of anesthesia in cesarean section of pregnant women with fetal distress because general

anesthesia does not require a long time to start the incision when compared to regional anesthesia.[6]

Response time for the implementation of cesarean section at Dr. Soetomo General Academic Hospital was >30 minutes, which was experienced by 85 patients (83%) while patients who underwent the operation for <30 minutes were 18 (17%). This differs from the defined time for classification of grade 1 emergency cesarean section in other cases, such as those with fetal bradycardia, umbilical cord prolapse, uterine rupture, placental abruption and pathological cardiotocography, which may take 30 minutes.[6] The infant outcome at Dr. Soetomo General Academic Hospital for the period 2015-2017 showed that most of the infants experienced severe asphyxia, consisting of 57 patients (56.3%).

Characteristics of pregnant women with fetal distress undergoing cesarean section and infant outcomes at Universitas Airlangga Hospital

In Universitas Airlangga Hospital, most patients had an age range of 20-30 years, as many as 4 patients (80%). All patients had gestational age at term (>37 weeks). The most common disease among pregnant women was hypertension in 3 patients (60%). Although most of the patients had hypertension, the patients arrived at >37 weeks' gestation age so the pregnancy termination was carried out at that time.

Like at Dr. Soetomo General Academic Hospital, in the most common type of anesthesia was general anesthesia in 4 patients (80%), while regional anesthesia was performed in 1 patient (20%). This is in accordance with a previous study which found that the choice of anesthesia in cesarean section in pregnant women with fetal distress is the general anesthesia because it does not require a long time to wait for the onset of drug action.[6]

Response time for cesarean section in the hospital. Universitas Airlangga was> 30 minutes in 3 patients (60%) and <30 minutes in 2 patients (40%). This differs from the time requirements for classification of grade 1 emergency cesarean section in cases including fetal bradycardia, umbilical cord prolapse, uterine rupture, placental abruption and pathological cardiotocography, which is 30 minutes.[7] Out of the baby at the hospital. Universitas Airlangga for the period 2015-2017 showed that all of them had moderate asphyxia.

Relation of response time for cesarean section with infant outcome

Data processing response time for cesarean section has a value of p=0.027 (p <0.05) which shows a significant correlation between the response time of cesarean section in fetal distress infants with fetal output, while between age and outcome the baby does not show a significant correlation with p=0.534 (p> 0.05).

One of the factors that can affect the response time in our study is related to the condition of the pregnant women when they arrived at the hospital.[8-10] From the data obtained from Dr. Soetomo General Academic Hospital, there were 20 pregnant women with fetal distress and underlying hypertension (preeclampsia, eclampsia, chronic HT) accompanied by pulmonary edema, while there were as many as 20 patients with heart defects. This caused delayed response time to carry out the procedure, which might be due to time needed to obtain supporting data such as laboratory examinations, chest radiographs and echocardiography. This additional examinations is highly necessary for the safety of the patient before surgery.[11-15] However, we did not obtain the data on the time needed for anesthetic preparations related to preoperative anesthesia, time to obtain effective action of the anesthetic agent, time for pediatrics time to arrive to the operating room, time for transportation for the patient to the operating room, and preparation time for the operating room, so this was a weakness of this study.

CONCLUSION

The response time obtained this study from both hospitals was more than 30 minutes, which indicated a low response time. The outcome of infants in both hospitals that showed varying degrees of asphyxia indicated that a long response time (> 30 minutes) could have an effect on infant outcome. These indicated there was significant correlation between caesarean section response time and fetal outcome. Further research is needed to analyze the response time associated with cesarean section in pregnant women with fetal distress using more valid and accurate data involving the time for anesthesia and pediatric preparation, patient transportation to the operating room, and preparation of the operating room.

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