

## Correlation between levels of troponin T (TnT), pH cord blood, and Apgar score in fetal distress and normal pregnancy

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**Abstract :** Fetal distress is a condition when fetus does not receive enough oxygen causing fetal asphyxia interrupting growth and development of fetus leading to fetal and neonatal death. Methods used in prevention of fetal distress have not showed significant result yet. Measurement of Troponin T (TnT) is suggested as an alternative approach through measurement of levels of neonatal cord blood. Levels of TnT in neonates with respiratory failure, cardiac dysfunction, and asphyxia were found higher compared to healthy ones. Maternal cardiac also affects in reducing oxygen supply into fetus. This study aimed to determine new methods in early detection of fetal distress during pregnancy through measurement of maternal TnT levels. **Method:** This is observational analytic study with cross-sectional design. Cord blood samples were carried out from patients with caesarian birth Level of TnT was measured by ELISA method and pH of cord blood was measured by pH meter. Calculations were done by statistical analysis. **Results:** It is found that levels of TnT were higher in fetal distress compared to control ( $p = 0.003$ ,  $p < 0.05$ ). Result showed pH of cord blood was lower in fetal distress compared to control ( $p = 0.040$ ,  $p < 0.05$ ). There was negative correlation between levels of TnT and pH cord blood, Apgar score in fetal distress. **Conclusion:** Information regarding correlation between levels of TnT and pH cord blood, Apgar score in fetal distress and normal pregnancy is expected as a new approach in early detection of fetal distress during pregnancy resulting proper prevention in fetal and neonatal mortality by reducing fetal distress.

**Keywords :** asphyxia, acidosis, fetal distress, hypoxia, troponint

### Introduction

Fetal distress is a term to describe when fetus does not receive enough oxygen causing fetal asphyxia (hypoxia and metabolic acidosis) interrupting growth and development of fetus leading to fetal death and

neonates.<sup>1</sup>Asphyxia is a condition of inadequate amount of oxygen (hypoxia), metabolic acidosis, and organ dysfunction as results of series of events in certain period.<sup>2</sup>

Fetal mortality occurrence was approximately 4 million worldwide at first month birth. Most incidences occur due to asphyxia, sepsis, and prematurity. Number of neonatal mortality remains higher in Indonesia among fellow ASEAN members. According to *Survei Demografidan Kesehatan Indonesia* in 2007 (SDKI 2007), neonatal mortality in Indonesia was approximately 19 deaths/1000 living birth, whereas fetal mortality was 34 deaths/1000 living birth. Respiratory failure remains major cause in neonatal mortality which is 37%.<sup>3</sup>

Prior detection of development risk is necessary in handling fetal distress. Monitoring of fetal wellbeing is a common method used in treating fetal distress such as measurement of parameters in fetus using cardiotocography (KTG), Apgar score, and pH of cord blood. However, currently method used does not seem to decrease neonatal mortality due to its low accuracy. Measurement with KTG is known resulting low validity and high false-positive. Measurement of fetal outcome with Apgar score has disadvantage in time and it is considered subjective. Biochemical disruption also occurs significantly prior to scoring. Several factors may affect Apgar score such as trauma, congenital anomaly, infection, hipoksiamhipovolemiam and preterm birth.

Biochemical methods in handling fetal distress are being developed. Troponin T (TnT) protein is widely used as a marker in detection of fetal distress. TnT is 35 kDa protein found in striated muscle fibers affecting muscle contractility.<sup>6</sup>TnT is a part of troponin protein complex interacting with tropomyocin regulating cardiac muscle contractility. TnT is not expressed in cord blood of healthy neonates. Previous studies showed levels of TnT in cord blood are increased in neonates followed by symptoms such as respiratory failure, asphyxia, and cardiac dysfunction.<sup>8</sup>TnT can be used as potential marker in determining damage in myocardium in adults, child, and fetus.<sup>9</sup>Cardiovascular tract is a fetal system which is responsible sending significant response on decreased amount of oxygen (hypoxia) and intrauterine growth restriction (IUGR).<sup>10</sup>TnT in maternal serum is suggested having predictive value in biochemical measurement of fetal distress. However, measurement of TnT in maternal serum is not effective in detecting possibility of fetal distress onset due to blood samples are carried out after birth. Measurement of TnT levels in maternal serum in laboratory also requires more time.

There are several factors generating inadequate oxygen into fetal body, one of which is maternal factor. Maternal health such as hypotension and aortal compression causes inadequate placenta perfusion from maternal side leading to reduced oxygen supply for fetus. Therefore, early detection of maternal factors increasing risk of fetal distress development is necessary. This study aimed to determine correlation between levels of maternal TnT and pH of blood cord and fetal outcome in fetal distress. It is expected to discover new method in early detection of fetal distress during pregnancy resulting proper prevention in fetal and neonatal mortality by reducing fetal distress.

## Experimental

Cord bloods were obtained from patients in accordance with criteria of fetal distress based on cardiotocography (KTG). Cord blood samples were carried out from patients with caesarian birth. Levels of TnT, pH, and Apgar were further measured immediately after birth.

Subjects were managed according to guidelines therapy of Obstetrics and Gynecology Faculty of Medicine Padjadjaran University HasanSadikin Hospital (FKUP/RSHS), Bandung, through some tests includes:(1) anamnesis; name, age, address, parity, first day of last haid, gestational age, previous hypertension record, current difficulties in pregnancy, and drugs currently used during pregnancy, (2) measurement of cord TnT levels was conducted through carrying blood samples from cord prior to operation using specific tube on negative vacutainer pressure with disposable syringe. Levels of TnT serum were measured with *high sensitivity indirect sandwich enzyme linked immunosorbent assay* (ELISA), (3) measurement of bloods pH from umbilical artery with pH meter in Laboratory of Clinical Pathology, Hasan Sadikin General Hospital. Apgar was immediately measured after delivery. Written informed consent was obtained from all participants. The ethical reviews boards of the Health Research Ethics Committee, Faculty of Medicine Padjadjaran University and Dr. HasanSadikin Hospital, Indonesia, approved this study.

## Results and Discussion

### Characteristics of Research Subjects

This research has 48 subjects involving 24 subjects with fetal distress and 24 subjects with normal fetus as controls. Characterization of the subjects in both groups has no significant difference in age, parity, and gestational age which is performed by T-test with confidence level 95% in both groups respectively; age  $p=0,319$ ; parity  $p=0,417$ ; and gestational age  $p=0,250$ . Characterization data is homogenous ( $p > 0,05$ ), as shown in Table1.

**Table1. Characteristic of Subjects**

| Characteristic                 | Group          |                | p-value |
|--------------------------------|----------------|----------------|---------|
|                                | Fetal distress | Normal         |         |
| <b>Age (years old)</b>         |                |                |         |
| Average $\pm$ SD               | 30.2 $\pm$ 5.2 | 28.3 $\pm$ 6.9 | 0.319*  |
| Range                          | 22-41          | 20-42          |         |
|                                |                |                |         |
| <b>Gestational age (weeks)</b> |                |                |         |
| Average $\pm$ SD               | 37.9 $\pm$ 1.3 | 37.0 $\pm$ 1.5 | 0.25*   |
| Range                          | 37-40          | 37-40          |         |
|                                |                |                |         |
| <b>Parity</b>                  |                |                |         |
| 1                              | 15             | 11             | 0.417** |
| >1                             | 9              | 13             |         |

Note: \* p-value was measured with unpaired T-tests;\*\* p-value with Chi square

**Table 2. Comparison between levels of Troponin-T and pH of cord bloods in fetal distress group and normal**

| Variables                 | Group              |                   | p-value |
|---------------------------|--------------------|-------------------|---------|
|                           | Fetal distress     | Normal            |         |
| <b>Troponin-T (ng/ml)</b> |                    |                   |         |
| Average $\pm$ SD          | 0.088 $\pm$ 0.0098 | 0.045 $\pm$ 0.084 | 0.003*  |
| Median                    | 0.06               | 0.007             |         |
| Range                     | 0.004-0.389        | 0.0-0.297         |         |
| N                         | 18                 | 24                |         |
| <b>pH</b>                 |                    |                   |         |
| Average $\pm$ SD          | 7.23 $\pm$ 0.13    | 7.30 $\pm$ 0.068  | 0.040** |
| Range                     | 6.94-7.28          | 7.15-7.44         |         |
| n                         | 12                 | 14                |         |

Note: \*p-value with Mann-Whitney; \*\*p-value with one-way T test

### Levels of Troponin T (TnT) and pH of Cord Blood

Table 2 shows comparison between levels of TnT and pH cord blood in fetal distress and normal. Table 2. shows research subjects involved consisted of 18 subjects with fetal distress and 24 subjects with normal fetus. Result showed levels of TnT were higher in fetal distress compared to control. There was no significant difference in levels of TnT between both group which was performed with Mann-Whitney test with confidence level 95% ( $p = 0.003$ ,  $p < 0.05$ ). Levels of TnT in cord blood were found higher in fetal distress compared to control.

TnT is not present in cord blood of healthy neonates. However, there is normal amount of TnT that might be express in healthy neonatal cord blood in small concentration on 0.050 ng/ml.<sup>7</sup> Levels of TnT in fetus

which undergo respiratory failure are higher compared to normal. It has been reported that increased levels of TnT is not commonly found in child fetus with respiratory failure. It is only found in fetus with development of systemic hypotension with requirement of inotrope therapy.<sup>7</sup>

Recent studies showed TnT is not expressed in fetal death due to respiratory failure as result of hypoxemia with difficulties of systemic hypotension. However, TnT is detected and gradually elevate to 0.175 ng/ml each 4 hours of neonates added.<sup>13</sup> In adults, levels of cardiac TnT are present 2 hours after cardiac dysfunction. The presence of TnT on cord blood at newly birth neonates indicates damage on myocardium during antenatal period.<sup>7</sup>

Expression of TnT is found increased significantly in neonated with high requirement of oxygen which undergo respiratory failure.<sup>13</sup> It concluded that expression of TnT is associated with requirement of oxygen. Guneset *al.* reported that fetus with asphyxia has higher levels of TnT than healthy ones. Levels of TnT in asphyxia fetus remain high until day 3 and day 7.

Research subjects of pH measurement in this study involved 12 subject with fetal distress and 14 subjects as controls. Result showed pH of cord blood was lower in fetal distress compared to control. There was no significant difference between both groups ( $p = 0.040$ ,  $p < 0.05$ ). pH value in cord blood was lower in fetal distress compared to control.

pH of cord blood is a marker used in determining hypoxia in fetus during delivery and necessary in decision making of intensive treatment. Range pH of cord blood in normal condition 7.25-7.28. pH in arterial cord blood  $< 7.20$  indicates acidosis onset, a condition of extremely high concentration of ion hydrogen in blood as indicator of hypoxia.<sup>4</sup>

Main source of hydrogen ion in fetus originate from carbonate acid and lactate acid. Carbonate acid originate from aerobic respiration, whereas lactate acid originate from anaerobic respiration. Excess lactate acid in fetus cannot be metabolized causing lactate to be flowed into maternal circulatory through placenta. Thus, concentration of lactate is found higher in cord artery than cord vein.

### **Correlation between levels of Troponin T (TnT), pH of cord blood, and Apgarscore in fetal distress and normal**

Table 3. shows correlation between levels of Troponin T, pH of cord blood, Apgar score in fetal distress and normal fetus. There was negative correlation between levels of TnT and pH cord blood, Apgar score in fetal distress ( $R_s = -0,57$ ,  $p = 0,86$ ). Neonates with fetal distress generate low Apgar score. It might be caused by inadequate amount of oxygen supply during its development causing low heartbeat, meconium aspiration, nuchal cord, long delivery, and disruption during birth. Inadequate fetal environment negatively affects its physiology and outcome indicated by low Apgar score.<sup>5</sup>

**Table 3. Correlation between Troponin-T (TnT-T), pH cord blood, and Apgar score in fetal distress**

| <b>Korelasi</b>  | <b>N</b> | <b>Koef Korelasi</b> | <b>Nilai -p</b> |
|------------------|----------|----------------------|-----------------|
| Trop T dengan Ph | 14       | -0,57                | 0.86            |

Note:  $r_s$  = Rank Spearman correlation coefficient

Apgar score is physically expressed in neonates, having disadvantage in time, and subjective measurement. Biochemical disruption occurs significantly prior to scoring. Parameters measured are affected by neonates physiology maturity. Healthy preterm neonates without asphyxia can result low score due its immaturity. Several factors may affect Apgar score such as trauma, congenital anomaly, infection, hipoksiamhipovolemiam and preterm birth.

Incidence of low Apgar score is inversely proportional to infant weight and limited to predict morbidity and mortality. Diagnosis of asphyxia is not well established depending on Apgar score.<sup>5</sup>

## Conclusion

Levels of Troponin TnT in fetal distress were higher compared to normal pregnancy. pH in pregnancy with fetal distress was lower than that in normal pregnancy. There is negative correlation between levels of TnT and pH cord bloods in fetal distress onset.

## Competing Interest

The authors declare that they have no competing interests.

## Author Contribution

ES, JCW and FFW carried out the samples collection, and in vitro studies, participated in the molecular assessment and drafted the manuscript. PNF, BH, AMM, AYP, and DDR participated in the design of the study and performed the statistical analysis. ES, JCW, FFW, BH, AMM and AYP conceived the study, and participated in its design and coordination and helped drafting the manuscript. All authors read and approved the final manuscript.

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