Instructions for the Authors

Coverage
The manuscripts should be prepared for one of the following article categories which are peer-reviewed:

- Clinical Research Article
- Experimental Study
- Case Report
- Technical Note
- Letter to the Editor

In addition, the journal includes article categories which do not require a peer review process but are prepared by the Editorial Board or consist of invited articles, titled as:

- Editorial
- Viewpoint Article
- Review Article
- Abstracts
- Announcements
- Erratum

Manuscript Evaluation
All submissions to Perinatal Journal must be original, unpublished, and not under the review of any other publication. This is recorded by the system automatically with the IP number, the date and time of submission. On behalf of all authors the corresponding author should state that all authors are responsible for the manuscripts. The name, date, and place of the relevant meeting should be stated if the submission is a work that was previously presented in a scientific meeting.

Following the initial review, manuscripts which have been accepted for consideration are reviewed by at least two reviewers. The Editors of the journal decide to accept or reject the manuscript considering the comments of the reviewers. They are authorized to reject or revise the manuscript, to suggest required corrections and changes upon the comments and suggestions of reviewers, and/or to correct or condense the text by permission of the corresponding author. They have also the right to reject a manuscript after authors’ revision. Author(s) should provide additional relevant data, documents, or information upon the editorial request if necessary.

Ethical Issues
All manuscripts presenting data obtained from studies involving human subjects must include a statement that the written informed consent of the participants was obtained and that the study was approved by an institutional ethics board or an equivalent body. This institutional approval should be submitted with the manuscript. Authors of case reports must submit the written informed consent of the subject(s) of the report or of the patient’s legal representatives for the publication of the manuscript. All studies should be carried out in accordance with the World Medical Association Declaration of Helsinki, covering the latest revision date. Patient confidentiality must be protected according to the universally accepted guidelines and rules. Manuscripts reporting the results of experimental studies on animals must include a statement that the study protocol was approved by the animal ethics committee of the institution and that the study was conducted in accordance with the internationally accepted guidelines, including the Universal Declaration of Animal Rights, European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Principles of Laboratory Animal Science, and the Handbook for the Care and Utilization of Laboratory Animals. The authors are strongly requested to send the approval of the ethics committee together with the manuscript. In addition, manuscripts on human and animal studies should describe procedures indicating the steps taken to eliminate pain and suffering.

The authors should also disclose all issues concerning financial relationship, conflict of interest, and competing interest that may potentially influence the results of the research or scientific judgment. All financial contributions or sponsorship, financial relations, and areas of conflict of interest should be clearly explained in the cover letter to the Editor-in-Chief at the time of submission, with full assurance that any related document will be submitted to the journal when requested. For the details of journal’s “Conflict of Interest Policy” please read the PDF document which includes “Conflicts of Interest Disclosure Statement”.

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Manuscript Preparation
In addition to the rules listed below, manuscripts to be published in Perinatal Journal should be in compliance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals published by International Committee of Medical Journal Editors (ICMJE) of which latest version is available at www.icmje.org.

Authors are requested to ensure that their manuscript follows the appropriate guidelines such as CONSORT for randomized controlled trials, STROBE for observational studies, STARD for diagnostic accuracy studies, and PRISMA for systematic reviews and meta-analyses, for the study design and reporting if applicable.

Authorship and Length of Texts
The author(s) must declare that they were involved in at least 3 of the 5 stages of the study stated in the “Acknowledgement of Authorship and Transfer of Copyright Agreement” as “designing the study”, “collecting the data”, “analyzing the data”, “writing the manuscript” and “confirming the accuracy of the data and the analyses”. Those who do not fulfill this prerequisite should not be stated as an author.

Original research articles base on clinical or experimental studies. The main text should not exceed 2500 words (max. 16 pages) and there should be a maximum 6 authors.

Case reports should illustrate interesting cases including their treatment options. The main text should not exceed 2000 words (max. 8 pages) and there should be a maximum 5 authors.

Viewpoint articles: Only by invitation and should be no more than 2000 words long (max. 8 pages).

Review articles: Only by invitation and should be no more than 4000-5000 words long (max. 20 pages).

Technical notes aims to present a newly diagnostic or therapeutic method. They should not exceed 2000 words (max. 8 pages) and include a maximum of 10 references.

Letters to the Editor should be no more than 500 words long (max. 2 pages) and include a maximum of 10 references.

Sections in the Manuscripts
Manuscripts should be designed in the following order: title page, abstract, main text, references, and tables, with each typeset on a separate page:

- Page 1 - Title page
- Page 2 - Abstract and key words
- Page 3 and next - Main text
- Next Page - References
- Next Page - Table heading and tables (each table should be placed in separate pages)
- Next Page - Figure legends and figures (each figure should be placed in separate pages)
- Last Page - Appendices (patient forms, surveys etc.)

Title page
This page should only include the title of the manuscript, which should be carefully chosen to better reflect the contents of the study. No unusual abbreviations should be used in the title of the manuscript. A short title as running heading not exceeding 40 characters should be given which is desired to appear on top part of continuing pages when journal is published.
Abstract page

Abstracts should not contain any abbreviation and references. They should be prepared under following designs.

— Abstracts of research articles should be max. 250 words and structured in four paragraphs using the following subtitles: Objective, Methods, Results, and Conclusion. Following the abstract, each abstract page should include max. 5 key words separated with comma and written in lower cases.

— Abstracts of case reports should be max. 125 words and structured in three paragraphs using the following subtitles: Objective, Case, Conclusion. Following the abstract, each abstract page should include max. 3 key words separated with comma and written in lower cases.

— Abstracts of review articles should be max. 300 words and presented not structured in one paragraph. Following the abstract, each abstract page should include max. 5 key words separated with comma and written in lower cases.

— Abstracts of technical notes should be max. 125 words and structured in three paragraphs using the following subtitles: Objective, Technique, Conclusion. Following the abstract, each abstract page should include max. 3 key words separated with comma and written in lower cases.

Main text:

The sections in main text are defined according to the manuscript type.

— In research articles, main text should consist of sections titled as “Introduction, Methods, Results, Discussion and Conclusion”. Each title may have subtitles. The categories of subtitles should be clearly defined.

The Introduction section should include a brief summary of the base of the work and clearly states the purpose of the study.

The Methods section should contain a detailed description of the material, the study design and clinical and laboratory tests, and statistical methods used. A statement regarding the ethical issues should also be given in this section.

The Results section should provide the main findings of the study. Data should be concisely presented, preferably in tables or graphs.

The Discussion section should mainly rely on the results derived from the study, with relevant citations from the most recent literature.

The Conclusion section should briefly and clearly present the conclusions derived from the results of the study. It should be in compliance with the aim of the work and and point out its application in clinical practice.

— In Case Reports, main text should be divided with the titles “Introduction, Case(s), Discussion”. Reported case(s) should be introduced clearly including the case story, and the results of laboratory tests should be given in table format as far as possible.

— The text of the reviews articles should follow the “Introduction” and be organized under subtitles which should clearly define the text’s context categorization. The Reviews are expected to include wide surveying of literature and reflect the author’s personal experiences as far as possible.

— The text of the technical note type of articles should be divided into “Introduction, Technical, Discussion”. The presented technic should be defined briefly under the related title, and include illustrations or figures as soon as possible.

— Letters to the Editor should not have titled sections. If there is a citation about a formerly published article within the text, reference(s) should be provided.

References

References used in the text should be directly related to the topic, as recent as possible and in enough numbers. They should be numbered in square brackets in the order in which they are mentioned in the text including Tables and Figures. Citation order should be checked carefully.

Only published articles or articles in press can be used in references. Unpublished data including conference papers or personal communications should not be used. Papers published in only electronic journals or in the preprint or online first issues of the electronic versions of conventional periodicals should be absolutely presented with DOI (digital object identifier) numbers.

Journal titles should be abbreviated according to the Index Medicus. All authors if six or fewer should be listed; otherwise, the first six and “et al.” should be written.

Direct use of references is strongly recommended and the authors may be asked to provide the first and last pages of certain references. Publication of the manuscript will be suspended until this request is fulfilled by the author(s).

The style and punctuation should follow the formats outlined below.


Figures and tables

All illustrations (photographs, graphics, and drawings) accompanying the manuscript should be referred to as “figure”. All figures should be numbered consecutively and mentioned in the text. Figure legends should be added at the end of the text as a separate section. Each figure should be prepared as a separate digital file in “.jpg” format, with a minimum 300 dpi or better resolution. All illustrations should be original. Illustrations published elsewhere should be submitted with the written permission of the original copyright holder. For recognizable photographs of human subjects, written permission signed by the patient or his/her legal representative should be submitted; otherwise, patient names or eyes must be blocked out to prevent identification. Microscopic photographs should include information on staining and magnification.

Each table should be prepared on a separate page with table heading on top of the table. Table heading should be added to the main text file on a separate page when a table is submitted as a supplementary file.

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For a swift peer review, Perinatal Journal operates a web-based submission, peer review and manuscript tracking system. Authors are required to submit their articles online. Details of how to submit online can be found at www.perinataljournal.com.

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The following list will be useful during the final check of a manuscript before submission:

1. Manuscript length (max. 4000 words for research articles)
2. Number of authors (max. 6 authors for research articles)
3. Title page (no unusual abbreviations)
4. Abstracts (max. 250 words for research articles)
5. Key words (max. 5 keys for research articles)
6. Main text (subtitles)
7. References (listed according to the rules of ICMJE)
8. Figures and tables (numbering; legends and headings; copyright info/permission)
9. Cover letter
10. Acknowledgement of Authorship and Transfer of Copyright Agreement (unsigned by all authors)
11. Conflicts of Interest Disclosure Statement (if necessary)
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VIEWPOINT

Delivery Methods in Multifetal Pregnancies

Mehmet Okan Özkaya, Mekin Sezik, Hakan Kaya

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Introduction

The frequency of the multifetal pregnancies is significantly increased as a result of the assisted reproduction techniques.1,2 With ovulation induction, twin births frequency multiplies 10 times approximately.2 The twin pregnancies form 1% of overall pregnancies while perinatal mortality rate is about 10%.3

The type of the delivery method is one of the most problematic issues in multifetal pregnancies. There are numerous controversies within the multifetal pregnancies for the delivery method. Most recent and comprehensive studies are will be enumerated in following section.

Planned Cesarean

The fact that whether all twin pregnancies which are delivered by cesarean decrease the perinatal mortality is a controversial subject. There exists some particular proof that the babies delivered by cesarean weight 1000 g and below and that is advantageous for Apgar scores perinatal mortality.4 As a result of a large scale meta-analysis on this subject, it is found that planned cesarean increases Apgar score only in fifth minute for breech presentation of the first fetus, however, there isn’t any difference between planned cesarean and normal confinement in perinatal mortality and morbidity.5 Consequently, except the excessive preterm twin cases, delivering all twin pregnancies doesn’t seem significant.

In twin pregnancies, the possibility that the fetus is delivered in vertex-vertex corresponds to 62%, 38% vertex-nonvertex, and 20% non vertex-nonvertex.5 In particular, if the first fetus is delivered in reverse presentation the delivery method is controversial. During a well-controlled study, the situations where the fetus is 1500 g and below, the breech delivery increases the neonatal mortality at 9.5 times.6 However, the breech delivery above 1500 g. (Apgar scores and neonatal mortality) seems as safe.7 In another multicentered study, when fetus in breech presentation is below 1500 g, Apgar score in fifth minute is reported low (p=0.008, OR 2.4, 95% CI 1.2-4.7). Within the same study, if the fetus is above 1500 g., there is no change in Apgar score for the vaginal confinement (p=0.76, OR 1.1, 95% CI 0.6-2.1) and reported that vaginal confinement could be made in these pregnancies.7

American College of Obstetricians and Gynecologists (ACOG) brings out that the cesarean should be preferred if twin presentation isn’t vertex independent from the weight of the fetuse. In a meta-analysis that confirms this idea, it was found that Apgar Score risk was increased at 50 % in fifth minute of abortion, (OR 0.47, 95 %, CI 0.26-0.88) and 1/3 when the first fetus is in breech presentation (OR 0.33, %95 CI 0.17-0.65).8

In consequence, for twin pregnancies, if the first fetus is in breech presentation and below 1500 g. and singleton pregnancy, the cesarean should be preferred.

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In these studies, when the first fetus is in breech presentation, for Apgar Score and neonatal mortality, vaginal and cesarean confinements give similar results. Besides, in well-controlled studies and meta-analysis, Apgar scores in cesarean are better in fifth minute. Therefore, in twin pregnancies the first fetus is in breech presentation, the cesarean is safer regardless of the weight.

**Presentation of the Second Fetus**

Another issue is related with the delivery methods that second fetus is nonvertex. According to another study, the presentation and fetal position of the second fetus don't have any difference for perinatal results except Apgar score in first minute. Breach presentation of the second fetus may not be a cesarean indication itself. However, in the cases left to the normal parturitions, there is a 10% "urgent cesarean for second fetus" rate. The breech presentation of the second fetus multiplies 4 times the urgent cesarean rate.

There are various publications that show that the second fetus has more risks, because of the delivery complications. In twins, the emergency cesarean is found associated with uterine rupture and infectious morbidity. In a recent and comprehensive study, it is showed that the vertex-breech twins delivered by cesarean method have a neonatal mortality rate comparable with vertex-vertex twins delivered by vaginal presentation. Yet, in the same study, interferelated with the previous findings, highest neonatal mortality rate is in vertex-breech presentations and it was observed in vaginal-emergency cesarean group (2.7/1000 gestation). In another study supporting the same findings, it is observed that neonatal mortality and morbidity in which were delivered by vaginal method or the first fetus vaginal and second by cesarean, are found higher than that both fetus are delivered by cesarean. In another study, it is compared delivering second fetus by cesarean in nonvertex position and both fetus by vaginal method. Apgar scores were higher in cesarean group and neonatal mortality was lower. Within the extent of the study, vaginal delivery is stated as dangerous for those type of twin pregnancies. However, in a study by Winn et al, it is reported that there is no difference in neonatal mortality and birth trauma while second fetus is in nonvertex, to implement cesarean to both fetus, vaginal delivery for the first fetus and cesarean to the second fetus and vaginal method for both fetus. Within this study, vaginal delivery is in particular specified as safe for 1500 g and above.

In consequence, for twin pregnancies that the second fetus is nonvertex, to left to the normal delivery, the need for emergency cesarean is and important issue. Even though no significant risk was assessed in retroactive studies, the "vertex–breech" presentations should be planned by taking into account the other factors as well as the patient. For these controversial situations, the weight of the fetus and the unfitness between the weights should be also considered.

In consequence, for twin pregnancies if the first fetus is in breech presentation and below 1500 g, the cesarean, is safer. In these studies, when the first fetus is in breech presentation, for Apgar Score and neonatal mortality, vaginal and cesarean confinements give similar results. Besides, in well-controlled studies and meta-analysis, Apgar scores in cesarean are better in fifth minute. Therefore, in twin pregnancies the first fetus is in breech presentation, the cesarean is safer regardless of the weight.

**Weight Difference between the Fetuses**

Another controversial issue for the twin pregnancies is that whether the birth weight differences matters in delivery method. In a recent study, it is found that the vaginal birth increases the neonatal mortality when the difference in fetus weights exceeds 40%. It was stated that the increase in risk started at 20% and becomes significant at 40%. Generally, the risk of the difference between the fetus weights brings out the fetal mortality and smaller fetus has more perinatal mortality risk. For perinatal results, 30% and more is assessed as clinically significant. In another study the twins below 1500 g limit were observed and for both cesarean and vaginal deliveries, the fetus with lower weight bears more risk in respiratory distress syndrome, and chronic respiratory system syndrome. Cesarean method seems more logic if the difference between birth weights of the twins is more than 20-30%. But there isn't any proof supporting this approach.
**Delivery in Vertex-Vertex Presentations**

Another issue is whether normal confinement in vertex-vertex presentations is always reliable. Vertex-vertex presentations may leave for normal delivery method. However, this isn’t always safest solution. In another study that examines the representation and delivery method in term twins, in case where emergency cesarean is needed for second fetus in vertex-vertex representation (vaginal – cesarean delivery) highest neonatal mortality (3.8/1000 live birth) has been observed. Further problems that the fetus cannot be engaged, delaying the birth may become a problem in vertex-vertex presentations. In vertex-vertex presentations in which no weight difference could be detected, there is a need for studies related to evaluate the necessity for cesarean in prenatal period.

**Triplet Pregnancies**

Except the twin fetal pregnancies, triplet and other multiple pregnancies are subject to a discussion on delivery method. In preliminary study, in case where first triplet is vertex, the fetus is delivered by vaginal method, and one-third of all triplets in the study (n= 23) are delivered (8 triplets) were delivered by vaginal parturition. There is no difference in neonatal morbidity and mortality between vaginal and cesarean. In contrary to this, another triplet pregnancy study showed that delivering overall three fetus by cesarean diminishes the neonatal mortality. For triplet pregnancies, cesarean will continue its validity as suggested delivery method until the reliability of normal birth proves itself in larger scale studies.

In multiple pregnancies, while the number of fetus multiplies, the mortality and morbidity for both mother and the fetus. In a comprehensive study, 44605 pregnancy cases were assessed and 1.3% twin, 0.1% triplet frequency was estimated. The most frequent perinatal complication, early parturition occurred in triplets 2 times comparing to the twins. Maternal mortality is estimated 35.8/100.000 for twins and 99/100.000 for triplets. Perinatal mortality is augmenting 2 times in triplets (115/1000 to 223/1000). In multiple pregnancies, perinatal and neonatal mortality are observed for the fetus that have 1500 and lower fetal weight and earlier than 27 months. As fetal and maternal prognosis worsen and increase premature risk while the number of the fetus multiplies, studies aiming to reduce the iatrogenic multiple pregnancies, gain importance.

**References**


Abstract

Objective: Measurements of umbilical cord acid-base status are routinely carried-out in many perinatology centers. Umbilical cord gas measurements and complementary, provide the clinician with information of patient assessment, therapeutic decision making and prognostication in NICU. The aim of this prospective study was to establish the normal range of umbilical artery gas parameters, acid-base status and lactate levels in term and preterm healthy newborns and their relationship between delivery mode.

Methods: Umbilical artery gas parameters from 108 healthy newborns (85 term, 23 preterm; 48 vaginal deliveries and 60 caesarean sections) which were followed-up in Neonatology Unit, were evaluated.

Results: Umbilical artery mean lactate levels were higher in preterm newborns than term newborns (29.4 ± 2.75, 21.0 ± 1.0 mg/dl, p<0.01). Umbilical artery mean pO2, sodium, chloride and osmolarity levels were lower in vaginal deliveries than caesarean section (p<0.05, p<0.001, p<0.01, p<0.01 respectively). Umbilical artery lactate levels were higher in vaginal deliveries (28.95 ± 1.65 mg/dl) than caesarean section (18.06 ± 0.99 mg/dl) (p<0.001). Umbilical artery pO2, ctO2 and sO2 levels were positively correlated with F02Hb, FCOHb levels and negatively correlated with FHHb and FmetHb levels. Umbilical artery P02, ctO2 and sO2 levels were positively correlated with pH levels and negatively correlated with pCO2 levels.

Conclusion: Umbilical artery blood gas parameters must be evaluated with the clinical and laboratory findings of the newborns.

Keywords: Umbilical artery, blood gas, delivery type, lactate, term, preterm.
Introduction

Blood pressure parameters and the evaluation of these parameters is one of the most important indicators for determining the clinical condition of the patient, treatment plan and prognosis. While the evaluation of blood gas parameters is an important investigation of all the patients in intensive care units, the fact that the physiology is different in the newborn period and changes quickly and using a small amount of blood increases the value of the investigation. Only the pH, carbon dioxide and acid-base and oxygen partial pressures were evaluated but today many blood gas parameters are evaluated together in order to evaluate oxygenation and acid-base balance. Blood gases are the most important tools to determine oxygenation, carbon dioxide homeostasis, acid-base balance and pulmonary functions efficiency. Blood gases are also an important diagnosis tool for leading oxygen and ventilator cure for respiratory distress of newborns and also for the illnesses relating with cardiac, renal and central nervous system. Betterments in the values of blood gases can be seen as an efficiency of the treatment.

Taking and evaluating the umbilical artery blood gases in the birth room has become a routine implementation for a quality newborn care. Especially evaluation of the newborn in the first hours, joint evaluation of traditional Apgar scoring and umbilical artery and blood gas parameters became important for early diagnosis approaches. Especially of the newborn with high risk and bad general condition, in cases such as shock, hypotension, peripheral vasoconstriction and acrocyanosis, capillary and blood gas values reflect the real data. Notwithstanding, with the increase of the parameters in the blood gas analysis, hypoxia evaluation is not made by Apgar score and umbilical artery pH value. Lactic acidemia developed by hypoxia or compensated acid-base unbalances can be stated, ideas can be developed whether the hypoxia is acute or chronic, which mechanism results the compensation. This study is done to determine the umbilical artery blood gas analysis results for term and preterm healthy newborn born in our clinic for the reason that the blood gas parameters in the context of evaluation increased and to evaluate the possible relationship between these parameters and type of birth.

Methods

Newborns monitored in neonatology service with the 5th minute Apgar score above 6, and having neonatal period without problems are included in the study. 2 cc arterial bloods were taken from all the newborns after the cord was clamped by an injector washed with heparin. Samples were reached to the laboratory in ten minutes in accordance with the cold chain. All the umbilical artery blood samples are investigated using the parameters in table 1 in our unit biochemistry laboratory with ABL Radiometer device. Cut-off value for the umbilical artery value for healthy newborns were determined 7.20 in previous studies, 108 newborns whose umbilical artery pH value is above that value were included in the study. Work group is grouped according to their gestation week and birth type.

All the statistical evaluation is done using SPSS for Windows 10.0 (IL, Chicago, USA). Umbilical artery blood gas parameters are given as average ± SEM. In order to compare the data between the groups, t test is used for independent groups, Pearson correlation analysis is used for correlations. p<0.05 value is considered significant statistically.

Results

85 terms, 23 preterm in total 108 newborns were included in the study. 48 of the cases were born by vaginal delivery and 60 had cesarean section. Characteristics of the term and preterm infants evaluated in the study are given in the Table 2. The 1st and 5th minute average Apgar scores of the preterm infants were lower than term infants (in order p<0.001 and p<0.001).

Without separating pregnancy week and birth week, average umbilical blood gas parameter values of the 108 newborns are given in Table 3. In the evaluation due to the pregnancy week, umbil-
Umbilical artery sodium values (p<0.05) was found higher for term infants, potassium and calcium values being in the normal border were found higher for preterm infants (in order p<0.01, p<0.05). Umbilical artery lactate levels were found higher for preterm infants than term infants (29.4±2.75, 21.0±1.0 mg/dl, p<0.01) (Table3).

For the infants born by vaginal delivery (n=48), umbilical artery average pO2, Na, Cl and osmolarity values were lower than the cesarean section infants (n=60) (in order p<0.05, p<0.001, p<0.01, p<0.01). Umbilical Artery average Hct, K, Ca, glucose levels were found higher for the infants born by vaginal birth than the cesarean section infants (in order p<0.05, p<0.05, p<0.01, p<0.01). Umbilical artery average lactate levels were found higher for the infants born by vaginal birth (28.95 ±1.65 mg/dl) than the average lactate levels of cesarean section infants (p<0.001) (Table 4).

Positive correlation was detected between oxygenation parameters pO2, ctO2, sO2 levels. Positive correlation for umbilical artery o2O2, ctO2 and sO2 levels and F02Hb and FCOHb levels, and negative correlation between FHHb and FmetHb levels were detected. Between umbilical artery Po0, ctO2 and sO2 levels and umbilical artery pH level a positive, and between pC02 level and negative correction was seen. F02Hb was positively correlated with pH and negatively correlated with pC02. FHHb was negatively correlated with pH and positively correlated with pC02. There was negative correlation between FmetHb and pH, p50c value showed negative correlation with pH (Table 4).

Table 1. Values from blood gas device and umbilical artery analysis.

<table>
<thead>
<tr>
<th>Blood gas values</th>
<th>pH, pO2, pCO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmeter values</td>
<td>cHb1, Hctc, sO2, F02Hb, FCOHb, FHHb, FmetHb</td>
</tr>
<tr>
<td>Electrolyte values</td>
<td>K, Na, Ca, Cl</td>
</tr>
<tr>
<td>Metabolic values</td>
<td>Glucose, lactate, bilirubin, mOsm</td>
</tr>
<tr>
<td>Oxygen condition</td>
<td>pO22, p50c2</td>
</tr>
<tr>
<td>Acid-base status</td>
<td>cBA2, cHCO3-, ABF1, SBE1</td>
</tr>
</tbody>
</table>

1. cHb: Is the total hemoglobin (Hb) concentration in blood. Total hemoglobin mainly includes all types pf hemoglobin; such as deoxy, oxy, carboxy, met- ve sulfhemoglobin.
   cHb=cO2Hb+cHHb+cCOHb+cMetHb
2. sO2: Oxygen saturation in the artery. sO2=cO2Hb/cHHb + cO2Hb
   sO2: Oxidized hemoglobin related with the oxygen carrying hemoglobin
   This parameter gives the best information when used related with cHb
3. F02Hb is defined as the ratio between (oxyhemoglobin n level _), O2Hb and cHb (cO2Hb/cHb) concentrations. It is calculated as follows:
   F02Hb=cO2Hb/cHb
   FCOHb=cCOHb/cHb
   FHHb=cHHb/cHb
   FmetHb=cMetHb/cHb
4. FC0Hb=Carboxy hemoglobin ratio
   FCOHb=cCOHb/cHb
6. FmetHb=methemoglobin ratio
7. ctO2: oxygen concentration in blood.
8. p50: Oxygen pressure in the half saturated blood. This parameter determines oxygen oscillation in the tissues and the position of the oxygen dissociation curve (ODC) which is essential.

Table 2. Characteristic of 108 infants who’s umbilical artery blood gas was analyzed.*

<table>
<thead>
<tr>
<th>Pregnancy week</th>
<th>Birth weight</th>
<th>Apgar score at 1st minute</th>
<th>Apgar score at 5th minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>All the newborns (n=108)</td>
<td>37.9 ± 0.2</td>
<td>3053.5 ± 68.0</td>
<td>8.28 ± 0.2</td>
</tr>
<tr>
<td>Term (n=85)</td>
<td>38.9 ± 0.1</td>
<td>3315.4 ± 80.4</td>
<td>8.65 ± 0.1**</td>
</tr>
<tr>
<td>Preterm (23)</td>
<td>33.6 ± 0.4</td>
<td>2041.4 ± 112.4</td>
<td>6.50 ± 0.6</td>
</tr>
<tr>
<td>Delivery type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal (n=48)</td>
<td>37.5 ± 0.4</td>
<td>2926.6 ± 110.9</td>
<td>8.52 ± 0.2</td>
</tr>
<tr>
<td>Cesarean (n=60)</td>
<td>38.2 ± 0.3</td>
<td>3152.8 ± 83.1</td>
<td>8.10 ± 0.2</td>
</tr>
</tbody>
</table>

* Values are given means standard deviation.
** p<0.001, term and preterm infants.
correlation between oxygenation parameters and parameters showing the acid-base status except of the positive correlation between umbilical artery s02 level and chase level.

Negative correlation of electrolyte values of Na and Cl with chase, HCO3, ABEC, SBEC and lactate and positive correlation of K and Ca with these values were detected (Table 4).

### Table 3. Umbilical artery blood gas parameters due to age and delivery type for all the work group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All newborns (n=108)</th>
<th>Newborns (n=108)</th>
<th>Term newborns (n=85)</th>
<th>Preterm newborns (n=23)</th>
<th>Vaginal delivery (n=48)</th>
<th>Cesarean section (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>min-max</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH</td>
<td>7.30 ± 0.01</td>
<td>7.211 ± 0.01</td>
<td>7.30 ± 0.01</td>
<td>7.30 ± 0.01</td>
<td>7.31 ± 0.01</td>
<td>7.29 ± 0.01</td>
</tr>
<tr>
<td>P02 (mmHg)</td>
<td>19.1 ± 0.7</td>
<td>6 ± 47</td>
<td>18.7 ± 0.7</td>
<td>20.8 ± 1.6</td>
<td>17.62 ± 0.89c</td>
<td>20.35 ± 0.99</td>
</tr>
<tr>
<td>PCO2 (mmHg)</td>
<td>43.0 ± 0.7</td>
<td>28.5 ± 65</td>
<td>43.7 ± 0.8</td>
<td>40.7 ± 1.5</td>
<td>42.3 ± 1.0</td>
<td>43.6 ± 1.1</td>
</tr>
<tr>
<td>CTHb g/dl</td>
<td>14.6 ± 0.2</td>
<td>8.1 ± 19.8</td>
<td>14.4 ± 0.2</td>
<td>15.1 ± 0.6</td>
<td>15.2 ± 0.3c</td>
<td>14.1 ± 0.3</td>
</tr>
<tr>
<td>Hctc (%)</td>
<td>44.6 ± 0.8</td>
<td>25.3 ± 60.4</td>
<td>44.1 ± 0.8</td>
<td>46.2 ± 1.8</td>
<td>46.7 ± 1.0c</td>
<td>42.8 ± 1.1</td>
</tr>
<tr>
<td>S02 (%)</td>
<td>37.6 ± 1.9</td>
<td>9.2 ± 96.8</td>
<td>36.5 ± 2.1</td>
<td>41.7 ± 3.7</td>
<td>35.5 ± 2.9</td>
<td>39.2 ± 2.4</td>
</tr>
<tr>
<td>P02Hb (%)</td>
<td>38.7 ± 1.9</td>
<td>9.6 ± 94.7</td>
<td>37.2 ± 2.1</td>
<td>44.1 ± 4.2</td>
<td>35.8 ± 2.9</td>
<td>40.8 ± 2.5</td>
</tr>
<tr>
<td>FCOHb (%)</td>
<td>1.02 ± 0.01</td>
<td>0 ± 6.4</td>
<td>1.00 ± 0.1</td>
<td>1.08 ± 0.1</td>
<td>0.95 ± 0.1</td>
<td>1.06 ± 0.1</td>
</tr>
<tr>
<td>FHHb (%)</td>
<td>58.8 ± 2.0</td>
<td>3.1 ± 89.6</td>
<td>59.9 ± 2.3</td>
<td>54.9 ± 3.7</td>
<td>61.4 ± 2.9</td>
<td>56.8 ± 2.7</td>
</tr>
<tr>
<td>FmetHb (%)</td>
<td>0.93 ± 0.01</td>
<td>0.2 ± 2.5</td>
<td>0.94 ± 0.01</td>
<td>0.9 ± 0.1</td>
<td>0.91 ± 0.01</td>
<td>0.94 ± 0.01</td>
</tr>
<tr>
<td>Ca (mEq/L)</td>
<td>2.9 ± 0.01</td>
<td>1.4 ± 3.93</td>
<td>2.83 ± 0.01a</td>
<td>3.15 ± 0.01</td>
<td>3.01 ± 0.01c</td>
<td>2.80 ± 0.01</td>
</tr>
<tr>
<td>Cna (mEq/L)</td>
<td>146.9 ± 1.1</td>
<td>123 ± 183</td>
<td>147.9 ± 1.3b</td>
<td>143.1 ± 1.25</td>
<td>142.6 ± 1.4d</td>
<td>150.2 ± 1.5</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>1.82 ± 0.01</td>
<td>0.2 ± 3.88</td>
<td>1.73 ± 0.01b</td>
<td>2.15 ± 0.17</td>
<td>2.12 ± 0.11e</td>
<td>1.58 ± 0.11</td>
</tr>
<tr>
<td>CCl (mEq/L)</td>
<td>111.6 ± 0.6</td>
<td>92 ± 127</td>
<td>111.9 ± 0.7a</td>
<td>110.3 ± 1.0</td>
<td>109.8 ± 0.8e</td>
<td>112.9 ± 0.9</td>
</tr>
<tr>
<td>C glucose (mg/dl)</td>
<td>64.6 ± 2.7</td>
<td>23 ± 163</td>
<td>62.8 ± 2.8</td>
<td>71.6 ± 7.3</td>
<td>74.1 ± 4.8e</td>
<td>57.4 ± 2.6</td>
</tr>
<tr>
<td>Laktat  (mg/dl)</td>
<td>22.8 ± 1.05</td>
<td>7 ± 56</td>
<td>21.0 ± 1.0</td>
<td>29.4 ± 2.75</td>
<td>28.9 ± 1.6d</td>
<td>18.0 ± 0.9</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>0.77 ± 0.01</td>
<td>0 ± 2.3</td>
<td>0.75 ± 0.01</td>
<td>0.81 ± 0.01</td>
<td>0.8 ± 0.01</td>
<td>0.7 ± 0.01</td>
</tr>
<tr>
<td>Mosm (mmol/kg)</td>
<td>295 ± 2.0</td>
<td>253 ± 367</td>
<td>296 ± 2.5</td>
<td>290.7 ± 2.6</td>
<td>288.5 ± 2.6e</td>
<td>300.1 ± 2.9</td>
</tr>
<tr>
<td>Ct02 (Vol%)</td>
<td>8.02 ± 0.4</td>
<td>1.9 ± 19.9</td>
<td>7.80 ± 0.4</td>
<td>8.90 ± 0.9</td>
<td>8.0 ± 0.6</td>
<td>8.0 ± 0.5</td>
</tr>
<tr>
<td>P50c (mmHg)</td>
<td>22.6 ± 0.3</td>
<td>17.5 ± 32.1</td>
<td>22.8 ± 0.3</td>
<td>21.9 ± 0.4</td>
<td>22.7 ± 0.5</td>
<td>22.6 ± 0.3</td>
</tr>
<tr>
<td>Cbaz (mmol/L)</td>
<td>-4.98 ± 0.3</td>
<td>-12.9 ± 7.9</td>
<td>-4.6 ± 0.4</td>
<td>-6.4 ± 0.6</td>
<td>-5.3 ± 0.4</td>
<td>-4.7 ± 0.5</td>
</tr>
<tr>
<td>HCO3 (mmol/L)</td>
<td>19.1 ± 0.3</td>
<td>13.7 ± 28</td>
<td>19.3 ± 0.3</td>
<td>18.5 ± 0.4</td>
<td>18.7 ± 0.3</td>
<td>19.5 ± 0.4</td>
</tr>
<tr>
<td>ABEC (mmol/L)</td>
<td>-5.2 ± 0.4</td>
<td>-12.8 ± 6</td>
<td>-4.9 ± 0.4</td>
<td>-5.9 ± 0.6</td>
<td>-5.3 ± 0.4</td>
<td>-5.1 ± 0.5</td>
</tr>
<tr>
<td>SBEC (mmol/L)</td>
<td>-4.86 ± 0.3</td>
<td>-12.6 ± 7.9</td>
<td>-4.6 ± 0.4</td>
<td>-5.8 ± 0.6</td>
<td>-5.1 ± 0.4</td>
<td>-4.6 ± 0.5</td>
</tr>
</tbody>
</table>

* Values are given means standard deviation. a. When p<0.001 term-preterm infants are compared, b. When p<0.05 term-preterm infants are compared, c. p<0.01 When vaginal deliveries and cesarean sections are compared, d. p<0.001 When vaginal deliveries and cesarean sections are compared.

### Table 4. Correlation analysis results of the data of oxygenation.

<table>
<thead>
<tr>
<th></th>
<th>p02</th>
<th>S02</th>
<th>ct02</th>
<th>F02Hb</th>
<th>FCOHb</th>
<th>FHHb</th>
<th>FmetHb</th>
</tr>
</thead>
<tbody>
<tr>
<td>p02</td>
<td>r=0.89</td>
<td>r=0.73</td>
<td>r=0.86</td>
<td>r=0.33</td>
<td>r=0.81</td>
<td>r=0.51</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>S02</td>
<td>r=0.764</td>
<td>r=0.96</td>
<td>r=0.42</td>
<td>r=0.84</td>
<td>r=0.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ct02</td>
<td>r=0.79</td>
<td>r=0.47</td>
<td>r=0.8</td>
<td>r=0.55</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F02Hb</td>
<td>r=0.39</td>
<td>r=0.86</td>
<td>r=0.53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FCOHb</td>
<td>r=0.43</td>
<td>r=0.33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHHb</td>
<td>r=0.55</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td></td>
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</tr>
</tbody>
</table>
Discussion

While Apgar scoring is taken as the major criteria in order to evaluate the condition of the newborn and to define the affective newborn classically, it is suggested that it is not efficient to evaluate the perinatal asphyxia defined as hypoxemia and metabolic acidosis only by Apgar scoring, and blood gas analysis should be taken into consideration for a more objective evaluation. Umbilical artery gives a better idea than umbilical vein for evaluation of fetal metabolic condition. Even though venous pH is normal, arterial acidemia can be detected. Umbilical artery can give an idea for fetal acid-base balance and also maternal acid-base balance and the effect of placental function. It will be appropriate that the reference values due to gestation week and birth type being determined and all the parameters being evaluated totally. For instance, pO2, ct02 and p50 are the respiratory and homothetic section to maintain oxygen for the tissue and they are the key parameters for using the useable oxygen in the artery. There is a complex relationship between these parameters; a change in one of the parameters can be compensated by the other two parameters. For instance, a patient with hypoxemia, if Hb concentration when pO2 become 56 mmHg and sO2 become 79%, patient will reach the useable of normal artery oxygen. On the other hand, if Hb concentration is low or there is dyshemoglobinemia for a patient with 56 mmHg pO2 and 79% sO2, oxygen usage will be low. For this reason, oxygen taking, carrying and release must be evaluated together for the appropriate diagnosis and treatment. In our study pO2 was lower but Hct was higher for the vaginal births and there was compensation.

In the studies about umbilical artery blood gas it is thought that there can be affects of some factors such as delivery type, gestation week and some other factors in addition to the differences between the countries and clinics. Dudenhausen et al found the lowest umbilical cord pH value 7.04 and percentile value 7.21 in their studies on 681 newborn. 10th percentile BE value was 7.21, 90th percentile pCO2 value was 62 mmHg. Helwig et al in their study on 16,060 newborns, average umbilical artery pH was 7.26, pCO2 was 52 mmHg, ABE was -4, PO2 was 177 mmHg. They showed that there was no relationship between delivery type and gestational week in this patient. Sener et al found average umbilical pH value of 7.26±0.083 in their study on 188 newborns born with spontaneous vaginal delivery. In our study, cases having pH value above 7.20 was taken, average pO2 was 19.1 mmHg (6-47 mmHg), BE average value was -4.97 (-12.9- 7.9).

PaO2 is the most important determiner of SO2 but it is not the only determiner. Factors affecting oxygen dissociation, curve at a certain pO2 are temperature, pH and pCO2. As it can be seen in our study, there are positive correlation between SO2 and pH and a negative correlation with pCO2. PO2 is the impulsive force for the oxygen molecules to enter into erythrocyte and bind to hemoglobin chemically, the higher pO2 and the higher SO2 will be. ct02 is a parameter showing the total number of oxygen molecules directly (bind to hemoglobin or not) different from PaO2 or SaO2, and it is directly related with hemoglobin content different from the other two variable. It is calculate by the part of the ctO2 bound to hemoglobin (HbX1.34XSaO2) and the dissolved part (.003XPaO2):

\[ \text{ctO2} = \text{Hb (g/dl) X1.34 ml O2/g Hb X SaO2 + PaO2 X (.003 ml O2/ Hg/dl)}. \]

For this reason, it is an expected finding that these parameters (pO2, ctO2 and SO2 and FO2Hb, FHHHb and FmetHb) can show correlation with each other as seen in our study.

It is important to determine the reason of low Apgar sore for premature infants and cord blood acid-base status for these infants. Ramin et al detected a difference of umbilical artery pH, pCO2, PO2, HCO3 and BE values between preterm and term infants. Arikan et al stated that the average pH values can be high for the preterm and low for post terms. But, researchers showed that there is no relationship between umbilical cord oxygen saturation and gestation and they are distributed in a wide range. We did not detected a difference.
between the values of umbilical artery pH, pCO2, PO2, HCO3 and BE values in our study. In a study in our country Benian et al12 detected a difference between term and preterm newborns similarly and stated that there no impact of pregnancy age for the cases without uteroplacental deficiency.

Another factor that can be effective on umbilical artery blood gas is the birth action and the delivery type. It is shown that even the duration between the cesarean is decided and exercised have importance on blood gas parameters.13 Nickelsen et al14 detected low acidosis or mixed respiratory / metabolic acidosis in the newborns born in the 2nd phase of the birth between 10-30th minute. It was shown that oxytoxin and birth induction have no effect on the cord blood gas analysis. It was shown that vacuum extractions and low forceps implementations are related with low pH and high CO2 levels but it was thought to be related with the diagnosis reasoned for this type of birth and not related with vacuum or forceps. Difference between artery and vein parameters were seen generally for the healthy newborns, it was seen to be low difference between artery and vein parameters for depressed infants. In our study, umbilical artery average pO2, Na, Cl and osmolarity values were lower for newborns born by vaginal delivery than the newborns born by cesarean section. Umbilical artery average Hct, K, Ca, glucose levels were higher for newborns born by vaginal birth than the newborns born by cesarean section. umbilical section Christian et al15 compared the infants born breech vaginal position and cephalic presentation, and found that cord blood pH values were low and pCO2 values were high for the infants born by vaginal position.

In recent years, in addition to traditional blood gas parameters, umbilical artery and lactate levels have been added to the evaluation. Lactic acid will accumulate because the cell transformed into anaerobic metabolism from aerobic metabolism in the tissue hypoxia. Metabolic acidosis resulting from lactic acid accumulation in the blood is a reason for hypoxia.16 Westgren et al17 found higher lactate levels for instrumental delivery and cesarean sections than the vaginal births. Lactate levels had positive correlation with fetal pH, hemoglobin, base gap, pCO2 and HCO3 and had negative correlation with morbidity and mortality. In our study, umbilical average lactate levels was found higher for infants born by vaginal delivery than the average lactate levels for infants born by cesarean section.

On the other hand, lactate can accumulate resulting from other reasons than hypoxia. Liver disease and some medicine and toxins can increase the blood lactate level in adults. In addition, raise in the blood pyruvate can also increase the lactate level. For this reason, it is a more proper approach to accept the lactic acidosis as a non-specific determiner of hypoxia. Some studies show that there is a weak correlation between the oxygen accession to the tissue and lactic acid levels. It was emphasized that lactic acidosis is not a sensitive determiner for hypoxia. This insensitivity can result from the fact that there is no linear relationship with lactic acid while the progressive hypoxia. Raised levels can be temporary because lactic acid is metabolized by the liver.17,19

The main reason why the electrolytes does not exist in the blood gas analysis is for the calculation of anion gap (anion gap=AG).5 Lorenz et al20 investigat-
tigated that anion gap when there is not metabol-
ic acidosis for the critically ill newborns and whether the metabolic acidosis is lactic acidosis of hypertrophic acidosis by anion gap. In the study by measuring lactic acid levels, 16 mmol/L or more anion gap was seen determiner for lactic acidosis, lower than 8 was seen determiner for no lactic aci-
dosis, and values between 8-16 mmol/L was seen that it was useless to distinguish the diagnosis. In our study, electrolyte values of Na and Cl had neg-
itive correlation with cbase, HC03, ABEC, SBEC and lactate, and K and Ca had positive correlation with these values. In our study, pH and base deficit had no correlation with pCO2, had negative correlation with Na, Cl and positive correlation with K and glucose.

In conclusion, umbilical artery blood gases can give objective results to evaluate oxygenation, and acid-base status and to define perinatal asphyxia. Data must be evaluated with the results from healthy newborns and change levels taken as base. Evaluating every component systemically in evalu-
ating and monitoring umbilical blood gases by knowing the interaction between them will be guiding.

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18. Kruger K, Kublickas M, Westgren M. Lactate in scalp and cord blood from fetuses with ominous fetal heart rate pat-
Relationship Between Umbilical Artery Doppler Investigations and Perinatal Outcome in Patients with HELLP Syndrome

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3Zekai Tahir Burak Maternity and Children’s Hospital, Ankara

Abstract
Objective: To investigate the association between umbilical artery Doppler studies and subsequent perinatal mortality in pregnancies with HELLP syndrome.

Methods: Seventy-seven women with HELLP syndrome were retrospectively evaluated regarding systole/diastole (S/D) ratios and presence of absent or reverse end-diastolic flow (AREDF) on umbilical artery Doppler velocimetry. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of S/D ≥5 and AREDV during umbilical artery doppler investigations for the prediction of perinatal mortality were calculated.

Results: Cesarean section rate was 76% (n=57). Indications for cesarean delivery were obstetric causes in 6 women (10.5%) and fetal distress or HELLP syndrome in the remaining patients. Prenatal loss rate was 18% (n=14). There were 4 (6.3%) neonatal deaths out of 63 live-born infants. Sensitivity, specificity, PPV, and NPV of S/D ratio ≥5 on umbilical artery doppler velocimetry for predicting subsequent perinatal mortality was 85.7%, 66.7%, 36.3%, and 95.5%, respectively. Sensitivity, specificity, PPV, and NPV of the presence of AREDV on umbilical artery Doppler velocimetry for predicting subsequent perinatal mortality was 71.4%, 82.5%, 47.6%, and 92.8%, respectively.

Conclusions: Umbilical artery Doppler investigations might be essential for evaluating the risk of perinatal mortality and timing of delivery in patients with HELLP syndrome. Normal umbilical blood flow in HELLP syndrome may demonstrate a low risk for perinatal mortality.

Keywords: HELLP syndrome, umbilical artery, Doppler investigations, perinatal mortality.

HELLP sendromlu hastalarda umbilikal arter Doppler incelemesinin perinatal sonuçlarla ilişkisi

Amaç: HELLP sendromlu hastalarda umbilikal arter Doppler inceleme sonuçlarının, perinatal ve postnatal dönem fetal yillik hali göstergeleri ile olan ilişkisini belirlemektir.

Yöntem: Yetmiş yedi HELLP sendromlu hasta retrospektif olarak incelendi. Doppler incelemesinde Sistol/Diastol (S/D) oranı ile diastolik akım yokluğu (DAY) ve ters akım (TA) varlığı durumları araştırıldı. Umbilikal arter Doppler incelemesinde S/D ≥5 ve DAYTA olması durumunun perinatal mortaliteyi belirleyebilmesindeki sensitivite, spesifite, pozitif prediktif değer (PPD) ve negatif prediktif değer (NPD) hesaplandı.

Bulgular: Sezaryen oranı %67.4 (57) idi. Sezaryen ile doğurtulanlardan 6 (%10.5)'sü obstetrik endikasyonlarla sezaryen olurken, geri kalanlardı endikasyonu fetal distress ve HELLP sendromuna bağlı maternal patolojiler oluştururdu. Toplam 77 hastanın 14’unde (%18) takip sırasında prenatal kayıp geçerleştirdi. Canlı doğan 63 bebekten 4 (%6.3)’ü postpartum dönemde kaybedildi. Umbilikal arter Doppler (UAD) S/D ≥5 olmasının perinatal mortalite riskini belirlemekdeki sensitivite %85.7, spesifite %66.7, PPD %36.3 ve NPD %95.5, UAD incelemesinde DAYTA olması durumunda ise sensitivite %71.4, spesifite %82.5, PPD %47.6 ve NPD %92.8 olarak saptandı.


Anahtar Sözcükler: HELLP sendromu, umbilikal arter, Doppler inceleme, perinatal mortalite.
Introduction

Preeclampsia is one of the most important complications of the pregnancy. Increase in the blood pressure and proteinuria in the preeclampsia is a rule. HELLP syndrome is a multi system illness with hemolysis, raised liver enzyme level and low thrombocyte count. HELLP syndrome is generally followed by preeclampsia and sometimes sporadic. Although define etiopathogenesis is not known, genetic closure, abnormal placentation, immunological pathologies and mother vascular endothelium dysfunction can play a role. It is known that HELLP syndrome has a relationship between raised perinatal mortality and fetal growth retardation (FBG).

It is shown that in the examination of umbilical artery Doppler (UAD), in the case of the absent or reverse end-diastolic flow (AREDF), some undesired consequences can happen such as intrauterine growth retardation or perinatal mortality. But there is not acidosis in all of the fetuses that AREDF is detected. Today, evaluation of umbilical blood stream plays an important role for the detection of feto-placental deficiency. Although there are some studies evaluating umbilical blood changes for pregnant with FBG and preeclampsia, this parameter is not studied efficiently for the patients with HELLP syndrome.

The objective of our study is to investigate the association between UAD investigation results and determinants of perinatal and postnatal period fetal well being.

Methods

77 patients with HELLP syndrome who hospitalized and cured in Department of Gynecology and Obstetrics of Isparta Suleyman Demirel University and Clinics Gynecology and Obstetrics of Maternity Hospital Isparta, and Ankara Zekai Tahir Burak Maternity and Children’s Hospital were investigated retrospectively. Some of the patients were affected by HELLP syndrome while they were monitored for preeclampsia or hypertension reasoning from pregnancy and some other patients were diagnosed as HELLP syndrome in their first time (AST≥ 70 U/L, thrombotic count < 150000/≥ and LHD > 150 U/L). All of the patients had the routine physical examination and obstetric ultrasonography, routine bio chemistry examination, complete urine analysis, hemogram, hematocrit, thrombosis count examinations. UAD examinations were practiced by the same ultrasonography devices (Medison Sonace 8800 and Kretz Technic Combison 420) for the patients diagnosed HELLP syndrome or developed HELLP syndrome while their monitoring. In the Doppler examination, Sistol/Diastol (S/D) ratio and absent of diastolic flow (ADF) or reverse flow (RF) were searched. It was examined whether there was chronic hypertension or diabetes in anamnesis, abortion history and chronic illness in family history. Patients were closely monitored beginning from the time hospitalized to the time they were discharged from hospital after birth. Non-stress test (NST) results, intrauterine fetal loss and post partum fetal loss ratios, convulsion ratios were determined while the monitoring.

In UAD investigation, sensitivity, specificity, positive predictive value (PPD) and negative predictive value (NPD) according to perinatal mortality of detected S/D ≥5 and AREDF were calculated. In addition, sensitivity, specificity, PPD and NPD in determining the probability of non-reactive NST for being S/D ≥5 in UAD investigation were calculated. Sensitivity, specificity, PPD and NPD for NST to determine perinatal mortality were determined. Student’s t-test was used for statistical analysis.

Results

Average age of the patients included in the study was 28.0±6.5 years, gravida was 2.4±1.8 and parity was 1.1±1.4. Demographical characterizes of the patients and laboratory and Doppler results are shown in the Table 1.

For 14 of the total 77 patients (18%), intrauterine fetal loss was seen while monitoring. 38 of the patients (49.3%) of the patients had female fetus, 39 of the (50.3%) of the patients had male fetus. 7 patients (9%) were diagnosed eclampsia. When anamneses were examined, 10 of the patients (13%) had abortion history, 4 of the patients (5.2%) had chronic hypertension and 9 of the patients (11.7%) had hypertension history in the family. 50 patients (65%) in total were cured with antihypertensive treatment and magnesium sulfate treatment. 20 of the patients (26%) had vaginal delivery and the other had cesarean section. 6 of the patients (10.5%) having cesarean section reasoned...
Sezik M et al., Doppler investigations and perinatal outcome in patients with HELLP syndrome

Doppler investigations are an important method to evaluate fetal well being in the intrauterine period. Abnormal Doppler results or AREDF detection is related with bad perinatal results. Perinatal mortality ratios reaching 80% was informed for AREDF developed cases. In the Doppler investigation in intrauterine period, besides umbilical artery, investigations of middle cerebral artery and uterine artery can also be made. In the studies of Lacin et al emphasized that UAD investigation results are better than middle cerebral artery in order to show perinatal results. Nevermore, it is stated that joint investigation of bilateral uterine artery, middle cerebral artery and umbilical artery is better for the estimation of the results of perinatal. Joern et al investigated parameters of umbilical artery and bilateral uterine artery Doppler for FBG and/or preeclampsia or HELLP syndrome patients in their studies. They detected that average birth week and birth weight decrease significantly with a Doppler distortion in one of these veins. In the same study, in the cases of Doppler distortion of double side uterine artery, 90% problem can develop for risky pregnancies, and this ratio is 72% for umbilical artery.

### Demographical characteristics, laboratory and Doppler results of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.0 ± 6.5</td>
</tr>
<tr>
<td>Gravida</td>
<td>2.4 ± 1.8</td>
</tr>
<tr>
<td>Parity</td>
<td>1.1 ± 1.4</td>
</tr>
<tr>
<td>Estimated fetal weight by the ultrasonography (g)</td>
<td>1606 ± 699</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>151.5 ± 15.3</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>97.9 ± 10.0</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.0 ± 2.02</td>
</tr>
<tr>
<td>Hemotocric (%)</td>
<td>39.0 ± 6.3</td>
</tr>
<tr>
<td>Fibrinojen (g/L)</td>
<td>455 ± 120.5</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>102.5 ± 131.6</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>75.6 ± 93.1</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dl)</td>
<td>0.7 ± 0.5</td>
</tr>
<tr>
<td>Thrombosis (/µL)</td>
<td>141.2 ± 65.9</td>
</tr>
<tr>
<td>Sodium (mmol/dl)</td>
<td>138.4 ± 4.0</td>
</tr>
<tr>
<td>Potassium (mmol/dl)</td>
<td>4.35 ± 0.5</td>
</tr>
<tr>
<td>Calcium (mmol/dl)</td>
<td>8.45 ± 0.8</td>
</tr>
<tr>
<td>Prothrombin Time (sec)</td>
<td>11.9 ± 1.04</td>
</tr>
<tr>
<td>Activity partial thromboplastin time (Sec)</td>
<td>34.2 ± 4.7</td>
</tr>
<tr>
<td>Urine protein for 24 hours (g)</td>
<td>341 ± 193</td>
</tr>
<tr>
<td>Serum protein (g/dl)</td>
<td>6.08 ± 0.8</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>2.98 ± 0.5</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.92 ± 0.4</td>
</tr>
</tbody>
</table>

### Sensitivity, specificity, PPD and NPD to determine perinatal mortality in the study.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPD</th>
<th>NPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical Doppler S/D ≥5</td>
<td>85.7</td>
<td>66.7</td>
<td>36.3</td>
<td>95.5</td>
</tr>
<tr>
<td>Umbilical artery DAYTA</td>
<td>71.4</td>
<td>82.5</td>
<td>47.6</td>
<td>92.8</td>
</tr>
<tr>
<td>NST non-reactive</td>
<td>100</td>
<td>71.4</td>
<td>43.8</td>
<td>100</td>
</tr>
</tbody>
</table>

**Sensitivity: %72.2, Specificity: %82.9, PPD: %78.8, NPD: %72.3**

### Values to determine non-reactive NST for being $S/D ≥5$ umbilical artery Doppler.

<table>
<thead>
<tr>
<th></th>
<th>NST non-active</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Umbilical Doppler S/D ≥5</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
</tr>
</tbody>
</table>

### Table 1.

<table>
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### Table 2.

<table>
<thead>
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### Table 3.
Consequently, it is emphasized that investigation of bilateral uterine artery is an indispensable method to determine fetal risk.13

In our study, UAD results, perinatal results and NST were evaluated for the patients hospitalized for HELPP syndrome or developed HELLP syndrome while monitoring. We detected that AREDF detection in the UAD investigation or S/D ≥5 have high sensitivity and specificity in order to determine perinatal mortality.

Spirilla et al searched umbilical artery S/D ratio and short term neonatal complications and neurological developments for the first two years for 582 monomer pregnancies (between 24-35 weeks). 45.7% of the patients had also FBG diagnosis. In this group of patients, neonatal death or cerebral palsy (p: 0.001) was seen at the ratio of 3.4% when S/D ratio is below 95 percent, 4.9% when it is 95 percent and above and 17.3% when AREDF develops.7 In our study, 18% fetus of the mothers with HELLP syndrome is lost in intrauterine period. 10 of them (71.4%) had S/D ratio of ≥5.74% of the patients had cesarean section, 89.5% of these had cesarean induction reasoned from fetal distress or maternal problems from HELLP syndrome.

Venous Doppler investigations were done in the literature. Ductus venosus is one of the most used veins for that. For 35 patients that AREDF was detected in UAD, short term results of ductus venosus and effect to birth timing were investigated. Short term results (such as artery pH, intraventricular bleeding, and mortality) showed that evaluation of ductus venosus Doppler pulsatility index is important. In the study, it is also important ductus venosus Doppler evaluation in order to determine fetal results and pregnancy timing for the pregnancies with AREDF in umbilical artery current.14

In the literature generally patients with preeclampsia or FBG are studied in arterial Doppler investigations.15,16 UAD examinations are not commonly used for the HELLP syndrome cases in order to evaluate perinatal results. High sensitivity (83%) and high specificity (80%) for the fetuses whose Doppler results is FBG to determine bad fetal condition is stated in the literature.17

In our study, fetal loss in intrauterine group with AREDF is 47.6% (10 of the total 21 patients); neonatal mortality is 18.2% (2 fetuses from total 21 patients). 12 of the fetuses in 32 patients with UAD S/D≥5 (37.5%) was lost in the intrauterine period, 3 of 20 live born fetuses (15%) was lost in the neonatal period. All of the 4 fetuses lost in the neonatal period were born in the 32nd pregnancy week. Similar to our study as in our study, for patients with AREDF in UAD investigation, high ratios of neonatal death was informed.16,18 In our study, prematurity should be effective for neonatal deaths, not the deficiency in Doppler examination. Indeed, AREDF detection in umbilical artery blood current may not have a separate effect on perinatal mortality after the chances such as FBG and premature is checked.15 The objective of the conservative approach to the cases with HELLP syndrome is to decrease perinatal mortality by gaining time with fetal maturation but in our study, 14 of the fetuses (18%) were lost during the conservative treatment. The reason for that can be the low pregnancy week of the cases and thus the insistence for continuing conservative treatment.

In the literature, it is stated that UAD result are not efficient to determine fetal well being and the seriousness of the preeclampsia (thrill, hypertension level and other) but in the cases of deficient Doppler, ratio of FBG and cesarean increases.20,21

HELLP syndrome is an important obstetric problem that can cause bad results both for the mother and the infant. Umbilical artery S/D ratio is ≥5 for approximately half of the pregnancies with HELLP syndrome. When umbilical artery S/D ratio is ≥5, high sensitivity and NPD ratios are detected for the determination of perinatal mortality. When AREDF is monitored in UAD examination, high specificity and NPD ratios are detected for the determination of perinatal mortality. Pregnancies with pathologic UAD examinations, pregnancies result earlier.
When the risks of HELLP syndrome are considered for mother and infant, UAD investigation of these pregnancies are important both for the determination of perinatal mortality risk and the timing of birth. We believe that when not only the evaluation of umbilical artery but also bilateral uterine artery and middle cerebral Doppler evaluation is made, perinatal and postnatal mortality and morbidity can be better determined.

References
Abstract

Objective: To evaluate the use of misoprostol in second and third trimester labor induction in women with previous cesarean delivery.

Methods: Women with previous cesarean delivery and normal controls seen for second and third trimester labor induction were randomly assigned to receive either misoprostol vaginally 50 µg or 100 µg every 6 hours until active phase of labor achieved. Primary outcome measures were uterine rupture, induction-delivery interval, vaginal delivery at 24 hours. Statistical analysis was performed with the ANOVA for continuous variables and the chi square and Fisher exact test for categorical variables. P<0.05 was considered significant.

Results: Three hundred and twenty three were randomised, with 67 with prior cesarean section and 256 controls. The two groups were comparable with respect to gestational age, birth weight, preinduction cervical length and total misoprostol dose. The mean induction-delivery interval was significantly longer for the prior cesarean group (61.9 ± 7.71 hours vs 26.3 ± 1.45 hours, p<0.001). Significantly more women in the control group were delivered within 24 hours (p<0.001). No uterine rupture was detected in the previous cesarean group.

Conclusion: In second and third trimester labor induction, the use of misoprostol in women with previous cesarean delivery was not associated with an excess of complications, side effects and cesarean delivery rates.

Keywords: Misoprostol, previous cesarean delivery, labor induction.

Eski sezaryenli kadınlarda II. ve III. trimesterde misoprostolle doğum induksiyonu: prospektif kontrolü çalışma

Amaç: Eski sezaryenli olgularda ikinci ve üçüncü trimesterde doğum induksiyonu için misoprostol kullanımını değerlendiririk.

Yöntem: Doğum induksiyonu nedeniyle değerlendirilen eski sezaryenli ve uterin skarı bulunmayan kontrol grubu 50 ve 100 µg misoprostol dozları için randomize edildi. Doğumun aktif fazına kadar 6 saat arayla vagen arka forniksine 50 ya da 100 µg misoprostol tablet uygulandı. Olgular uterin rüptür, induksiyon-doğum aralığı ve 24 saatte vaginal doğum gibi sonuçlar yönünden değerlendirildi. İstatistik analiz SPSS 10.0 programı ile sürekli değişkenler için ANOVA ve kategorik değişkenler için kare ve Fisher kesin olasılık testi ile yapıldı, p<0.05 anlamlı olarak kabul edildi.

Bulgular: 67’si eski sezaryenli 256’sı kontrol olmak üzere 323 gebe iki ayrı misoprostol dozu için randomize edildi. Her iki grup gebeliğin haftası, doğum ağrılığı, induksiyon öncesi servikal uzunluk ve toplam misoprostol dozu açısından benzerdi. Ortalama induksiyon-doğum aralığı eski sezaryenli olgularda belirgin olarak uzun bulundu (61.9 ± 7.71 saat; 26.3 ± 1.45 saat, p<0.001). 24 saat içinde doğum oranını kontrol grubundaki gebeler de anlamli şekilde daha fazlaydı (p<0.001). Eski sezaryenli grupta uterin rüptür görülmedi.

Sonuç: Ikinci ve üçüncü trimesterde eski sezaryenli olgularda misoprostol doğum induksiyonu kompleksiyon, yan etki ve sezaryen doğum oranları yönünden kontrol grubuna göre farklılık göstermemiştir. Ancak induksiyon-doğum aralığı eski sezaryenli olgularda belirgin şekilde uzun bulunmuştur.

Anahtar Sözcüklar: Misoprostol, eski sezaryen, doğum induksiyonu.
Introduction

By increasing of prenatal ultrasonographic diagnostic possibilities, determination of fetal abnormalities before birth confront us the ending of pregnancy in lethal or severe fetal abnormalities as a serious choice. As similar, it is also necessary to ending the pregnancy in pregnancies complicated with intrauterine fetal death (IUFD). In recent years, cesarian section ratios were also increased quickly in our country as in the world. We confront this as an increase in pregnancy termination and delivery induction necessity in old cesarean section cases because of fetal abnormality or IUFD. It is not clear that what is the most appropriate induction method in this type of cases. Misoprostol is a synthetic prostaglandin E1 analog and it is used widely in second trimester pregnancy terminating and delivery induction. In the literature, there is no sufficient study related to efficacy and reliability of delivery induction in old cesarean section cases. For this reason, we performed a randomized prospective study to investigate the reliability and efficacy of misoprostol in old cesarean section cases in II. and III. trimesters in our unit.

Methods

This randomized controlled prospective study is performed between November 2001 and March 2005 dates at Perinatology Clinic. During the study pregnancy termination and delivery induction is performed using 4 different misoprostol (Cytotec, Ali Raif, TR) doses in 62 pregnant because of fetal abnormality, IUFD and severe preeclampsia. Pregnancy termination decision because of fetal abnormality is taken at a council of branch specialists of obstetrics and gynecology, pediatric surgery and chiefly pediatric Cardiology, developmental neurology, pediatric nephrology and neonatology and also with the participation of the family. Study is approved by ethic committee and informed acknowledgement form is taken from all of the pregnant. 238 out of 562 misoprostol induction used pregnant were excluded out of study because they were belong to 200 and 400 µg misoprostol protocol, and one pregnant was excluded because she had previous birth by classic incisional cesarean section. Residual of 323 pregnant were divided into two groups as old cesarean section and control groups and they were randomized for 50 and 100 microgram vaginal misoprostol application. The induction was started with 50 microgram for the patients admitted to clinic on odd days of the month and 100 microgram misoprostol for the patients hospitalized on even days of the month. According to randomization divided tablets of 50 or 100 microgram misoprostol tablets are placed to the posterior vaginal fornices every 6 hours. Cervices length was measured by transvaginal ultrasonography prior to this transaction and Bishop scores were recorded by vaginal examination. Following misoprostol dose was not administered to patients that determined in active phase. Additional methods such as extra-amniotic rivanol application by transcervical Foley catheter, oxytocin administration or increase in the misoprostol dose is applied to the cases that birth was not occurred within 48 hours during the whole study period. Parameters such as demographic data related to cases, pregnancy week, baby birth weight, induction-birth interval, total misoprostol dose, induction indication, side effect, additional method usage, vaginal delivery in 24 hours and complications due to intervention (uterine rupture, postpartum bleeding causing transfusion and placental retention) were recorded. Statistical analyses with SPSS 10.0 was made with using ANOVA for numeric variations and chi square or Fisher accurate probability test for categorical variations.

Results

67 cases (20.7%) accepted to study were old cesarean section. 172 cases (53.3%) because of fetal abnormality, 120 cases (37.2%) because of IUFD and 31 cases because of severe preeclampsia were administered delivery induction with misoprostol or were taken indication of pregnancy termination. There was not observed any difference about maternal age between old cesarean section cases that applied induction with misoprostol and control groups. Despite this, it was observed that parity was significantly high in old cesarean section group as expected (p<0.001) when compared to control group. Pregnancy age was calculated based upon the last menstruation date (LMD) and if LMD is not known it was calculated based upon early prenancy ultrasonography.
Average pregnancy age was 24 weeks during birth for both two groups. There was no significant difference between old cesarean sectio pregnant that were administered misoprostol induction and control group about numerical variations such as birth weight, Bishop score, cervices length before induction and total misoprostol dose used. Although mean time from induction to birth was significantly longer in cases with old cesarean sectio (61.9 ± 7.71 hours) than control group (26.3 ± 1.45 hours) (p<0.001). 319 (98.8%) of 323 pregnant included in the study pregnancy ended with vaginal route. There was no difference about vaginal deliveries after induction between two groups. When the probability of vaginal delivery in first 24 hours after induction is examined it is observed that 143 pregnant (44.3%) gave a birth after 24 hours. When the ratios of vaginal delivery in 24 hours is compared between two groups, it is found that this ratio was significantly low in old cesarean section when compared to control group (p<0.001). When two different misoprostol doses (50 and 100 µg) administered to old cesarean section and control group is examined, it is obvious that 100 µg misoprostol protocol was used significantly more in control group (Table 1).

While there is no side effect in 92.9% of cases due to misoprostol, in 17 cases (5.3%) nausea-vomitting, in 4 cases (1.2%) fever and in 2 cases (0.6%) diarrhea are determined. There is no significant difference about side effects due to misoprostol usage between groups. Additional method is used in 49 cases (15.2%) because birth didn’t occur within 48 hours after induction. Additional method is significantly more used in old cesarean section cases according to control group (p<0.001). When complications due to misoprostol induction are evaluated in old cesarean section cases, it is determined in 2 cases (2.9%) postpartum bleeding necessitating blood transfusion and in 2 cases (2.9%) placental retention. It is strange that there exists one case (0.3%) of uterine rupture due to delivery induction with misoprostol in control group. Furthermore, there is 3 cases (1.1%) of placental retention in control group. It is not found any significant difference about complications due to misoprostol between two groups.

**Discussion**

There is a marked acceleration in cesarean sections today. Its one of natural reflections to the obstetrical applications is increasing in requirement of pregnancy termination and delivery induction in pregnants with old cesarean section. There are limited number of studies in literature concerning efficacy and safety of delivery induction in old cesarean sectio cases. Misoprostol is a prostaglandin E1 analogue and is started to be used in an increasing frequency with the aim of delivery induction. Generally, it is mostly found studies related to termination of II. trimester pregnancies with misoprostol. One of the results obtained from our study is induction-birth interval and >24 hours vaginal delivery rates are found significantly high in old cesarean section cases induced with misoprostol. When looked at myometrial contractility and cervical maturation; it is obvious that suggesting a mechanism explaining

**Table 1.** Results concerning nominal measurements.

<table>
<thead>
<tr>
<th></th>
<th>Old sectio n (%)</th>
<th>Control n (%)</th>
<th>OR 95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiparity</td>
<td>65 (100.0)</td>
<td>128 (49.8)</td>
<td>32.7 (7.85-136.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Active phase success in 12 hours</td>
<td>38 (56.7)</td>
<td>157 (61.0)</td>
<td>0.83 (0.48-1.43)</td>
<td>0.51</td>
</tr>
<tr>
<td>Misoprostol dose (100 µg)</td>
<td>36 (53.7)</td>
<td>208 (80.9)</td>
<td>0.27 (0.15-0.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vaginal delivery (&gt;24 saat)</td>
<td>23 (34.3)</td>
<td>158 (61.4)</td>
<td>0.32 (0.18-0.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vaginal delivery (toplam)</td>
<td>65 (97.0)</td>
<td>255 (99.2)</td>
<td>3.92 (0.54-28.38)</td>
<td>0.19</td>
</tr>
<tr>
<td>Additional method requirement</td>
<td>20 (29.8)</td>
<td>29 (11.2)</td>
<td>3.34 (1.74-6.41)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
the late response of scarred uterus to misoprostol induction is very hard. When we limited the analysis to evaluating the succession of entering to the active phase of delivery action in cases induced with misoprostol in 12 hours because of that reason, the obtained result indicates that there is no difference between both groups. This makes us to think that real prolongation in induction-birth interval occurs after entering the active phase in old cesarean section cases. Using additional method in old cesarean section cases much more also supports this. It must don’t forget that implementers may have a prejudice of choice as not administrating the next dose of misoprostol to the old cesarean section group although pregnant has not entered to active phase with worry of rupture. But, the most important thing is significantly more usage of 100 µg misoprostol protocol in control group according to old cesarean section group.

The most severe complication is uterine rupture in old cesarean section cases administered delivery induction in second or III. trimester. There is found a few data in literature about results and complications of medical pregnancy termination and delivery induction in old cesarean section cases. It is not known true incidences related to complications such as uterine rupture or hysterectomy. It is reported that incidence of uterine rupture following induction is 0.2% - 0.9% in literature. However, heterogen structure of cases, differences in rupture definition and classification, different induction methods and protocols are limiting the evaluation of uterine rupture incidence. According to a study by Lydon-Rochelle et al to show the true increase in risk of uterine rupture related to induction with prostaglandines, sample size of the study must be 10,000 women.

In our previous study that we evaluated misoprostol induction in old cesarean section cases, the uterine rupture incidence is reported as a high ratio of 9%. There was no uterine rupture in old cesarean section group in this study and it can be explained with factors such as high misoprostol dose used in previous study, greater pregnancy week, oral misoprostol maintenance protocol, lack of experience concerning misoprostol induction. Daskalakis et al showed that the main cause for the low risk of rupture related to misoprostol induction in old cesarean sectio cases was that all of the cases were <24 pregnancy week. Kayani et al reported the uterine rupture risk related to induction is between 1-5% and determined that risk of uterine rupture related to delivery induction in old cesarean section cases who had not vaginal delivery previously was higher.

**Conclusion**

This study ensured the evaluation of delivery induction with misoprostol in old cesarean section cases in same center even so at different dates and with different methodologies. In conclusion, complication, side effect and vaginal birth rates are similar to the control group in delivery induction with misoprostol in old cesarean section cases because of fetal abnormalities and IUFD in II. and III. trimesters but, it is understood that induction-birth interval is longer in old cesarean section cases. There is need for randomized controlled prospective studies including sufficient number of cases in order to obtain reliable evidences about effect of delivery induction with misoprostol in old cesarean section cases to the rate of uterine rupture.

**References**


Vaginal Birth After Cesarean Section: 
Is It Safe?

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Abstract

Objective: Our goal was to analyse the effects of trial of labor on fetal and maternal outcomes among women with single previous lower segment cesarean delivery.

Methods: 124 patients following a single prior cesarean delivery were selected prospectively for trial of labor between 1.1.2002-30.4.2004. The inclusion criteria were, single and alive fetuses with vertex presentation, estimated fetal weight lower than 4000 g and greater than 28 weeks pregnancies' and whose cervical effacement was 80% and dilatations over 5 cm at first examination. The patients who had cephalopelvic disproportion or classic uterine incision and whose previous indication was cephalo-pelvic disproportion were excluded from the study. During trial of labor induction was not used and the labor was followed up by continuous external cardiotocography.

Results: The mean age of the cases was 27.4 ± 4.47 years, the mean gestational week was 33 ± 4 weeks, and the mean fetal weight was 2312 ± 410 g. At admission the mean servical dilatation was 4.68 ± 1.3 cm. In one case complete and in two cases partial uterine rupture from previous scar tissues occurred and immediate laparatomy was performed. The overall rate of uterine rupture was in %2.4 of the cases. Perinatal morbidity was established to be 13%, without any perinatal mortality.

Conclusion: In view of the fact that primary cesarean rates can be reduced if their actual indications are considered, vaginal birth after single cesarean may be considered as an amenable and acceptable method in tertiary clinics with adequate facilities for the mother and the newborn in carefully selected cases.

Keywords: Vaginal birth, cesarean section, uterine rupture.

Sezaryen sonrası vajinal doğum: güvenli midir?

Amaç: Alt segment transvers ınzizyon ile geçirilmiş tek sezaryen operasyonu olan oşteş, vajinal doğumun, fetal ve maternal prognoz üzerine olan etkisinin araştırılması.


Bulgular: Sezaryen sonrası vajinal doğum (SSVD) yapılan hastaların yaş ortalama 27.4 ± 4.47, ortalama gebelik haftaları 33 ± 4 hafta, ortalama bebek ağırlığı 2312 ± 410 g olarak saptandı. Hastaların kabulü sırasında pelvik muayenelerinde; ortalamalar servikal açıklıklar %4.68 ± 1.3 cm ve silinmeleri ise > %75 olarak gözlandı. Bir olgu da alt segment eski ınzizyonun bir önceki komplet rüptürü, 2 olguda ise parsiyel rüptür tespit edildi ve acil laparatomye alındı. Post operatif takip sorunsuzdu. Tüm olguların % %2.4 idi. 16 yenidoğan solunum sikintisi nedeniyle yenidoğan ünitemizce konsulte edildi. Perinatal morbidity %13 olarak saptandı. Perinatal mortalite gözlenmedi.

Sonuç: Primer sezaryen oranlarının gerçek endikasyonlarının kullanılması ile azaltılabileceği görülüğünden hareketle, 'sezaryen sonrası vajinal doğum'; dikdörtgen seçilmiş olgularda, anne ve yenidoğan için yeterli donanım ve bakım koşullarının olduğu tersiyer referans kliniklerinde uygulanabilir ve kablo edilebilir bir yöntem olarak görülmektedir.

Anahtar Sözcükler: Vajinal doğum, sezaryen uterus rüptürü.
Introduction

For the first time, Edwin B. Cragin declared that the cases having one time cesarean section should have the cesarean section in their following pregnancy.1 Although there have been developments in the obstetrical practice until that years, the question that in which way a patient having a cesarean section previously should delivery is not yet answered.

Ratio of cesarean section was 2-5% in 1950’s; it increased to 25-30% in 1990’s. However, neonatal mobility and mortality ratio did not significantly decrease.2 In recent decade, many researchers supported the trail of vaginal birth for selected cases in order to decrease the number of unnecessary abdominal births and increase the number of vaginal births after cesarean section.3,4 Wide multi-centered studies showed that the vaginal birth after cesarean section can reach success ratios of 60-90% by selecting the correct patient. This application, at the same time, decreased the hospitalization duration and ratio of postpartum infections.2,4 But, there are two fundamental problems for the trial of labor and practice of vaginal birth after cesarean section. These are the unsuccessfulness of the vaginal birth and uterine rupture.5 Uterine rupture is a serious complication which can cause the rise of fetal mortality and mobility.6

The objective of this study is to analyze the effects of trial of labor on fetal and maternal outcomes among women with single previous lower segment cesarean delivery.

Methods

This study is carried on 124 patients following a single prior cesarean delivery previously selected prospectively for trial of labor between 1.1.2002- 30.4.2004. The criteria to be included to the study were, single and alive fetuses with vertex presentation, fetal weight lower than 4000 gram estimated by ultrasonography and Leopold maneuver. The patients who had classic or T uterine incision and whose first cesarean indication was caused by cephalo-pelvic disproportion and abnormal labor progress were excluded from the study.

For the pregnancies older than 28th pregnancy week, cases having cervical effacement of 80%, cervical dilatations above 5 cm are included in the study. Under 28th week, early phases of the pregnancy is included in the study. Patients under 26th pregnancy week are not included in the study. In this type of cases, vaginal birth is tried firstly as it is stated in our hospital protocol. The entire patient and patient’s caregivers were informed by the work group and written permission approval was taken. There were obstetrician, neonatolog and anesthesiologist in the team all the time.

Trial of labor was followed continuously for fetal heart trace and spontaneous uterine contractions externally. Amniotomy was not exercised until effacement and partiation was completed in membrane intact cases. Induction with oxytocin or augmentation was not implemented during the vaginal birth monitoring. Intervened birth was practiced for the cased by vacuum and/or forceps if it was needed.

Perineum, vagina, collum and cavum uteri check was done for case having vaginal birth.

Perinatal goodness was evaluated by birth weight, APGAR scores of first and 5th minutes and clinical examinations of the newborns. New born cases showing respiratory distress findings and in neonatal care unit were determined and monitored.

All of the data belonging to the cases were evaluated on computer. Statistical analysis were discussed using SPSS (11.05 version) as descriptive and frequency analysis.

Results

Average age of the patients having trial of labor after cesarean (C/S) was 27.4±4.47, average pregnancy weeks was 33±4 weeks and average newborn weight was 2312±410 gram (Table 1). Presentation of patients according to their pregnancy weeks are presented in Table 2.
It is seen that 43.5% of the cases was in the pregnancy weeks of 34-37 weeks. When the cases decided to make vaginal birth after a cesarean is evaluated according to their first C/S inductions; 53.22% of the cases positive construction stress test, 40.32% of the cases primigravid breech presentation, 4.03% of the cases hypertension, preeclampsia, intrauterine growth restriction (IUGR), 5.41% of the cases twin pregnancy (breech-vertex presentation) (Table 3).

Three patients gave birth with the vacuum. In the routine uterine cavity investigation after the birth, uterus ruptures were detected in the 2.4% (3/124) of the cases. In one 29 years old case having a 3820 gram baby, complete rupture was detected, in 2 cases 27 and 30 years old having 3150 and 3460 gram baby, partial rupture was detected in the scar place of the bottom segment old utter. These three cases in the 37th and 38th week of pregnancy were urgently taken to laparotomy. C/S inductions of these cases in their first births were fetal distress. Rupture place was primarily remedied. These paints were transfused 2 units of new blood to each because of their low hemogram values (7.5 g/dl, 7 g/dl and 6.9 g/dl). There were no early complications concerning anesthesia and complication in the port operative period. They were discharged from hospital without ant problems.

When the cases are evaluated according to their pregnancy intervals, it is seen that period between the pregnancies were shorter than 20 months in 17.74% of the cases (22/124). 2.4% (3/124) of the cases that we detected uterus rupture was also included in that group. In addition, when new born weights of the first cesarean birth and this vaginal birth is compared, it is seen that the weight of the new born was more in the cases that we detected uterus rupture (2540±426 g to 3466±354 g) p< 0.05.

APGAR score of the one hundred eight (87.09%) newborn in the1st minute, 7 of them in the 7th minute were above 9. APGAR scores of the 1st and 5th minutes of 16 newborn were in order 2-6 and 4-8 limit. 16 newborns were consulted

| Table 1. Demographical and clinical characteristics of the cases. |
|------------------|-------------------|
| **Value interval** | **Means ± standard deviation** |
| Age | 21 - 40 years | 27.4 ± 4.7 years |
| Pregnancy week | 26 - 40 weeks | 33 ± 4 weeks |
| Newborn weight | 960 - 3820 g | 312 ± 410 g |
|Activity duration | 30 min - 20 hours | 6.5 ± 2.4 hours |
| Dilatation | 1 cm - 10 cm | 4.68 ± 2.25 cm |
| Gravida | 2 - 7 | 3.59 ± 1.23 |
| Parity | 1 - 4 | 2.27 ± 0.54 |

| Table 2. Distribution of the cases to the weeks. |
|------------------|-------------------|
| **Pregnancy week** | **N=124** |
| 38 - 40 week | 30 |
| 34 - 37 week | 54 |
| 30 - 33 week | 32 |
| 26 - 29 week | 8 |

| Total | 124 |

| Table 3. Distribution of first cesarean inductions to weeks. |
|------------------|-------------------|
| **Pregnancy week** | **Fetal distress** | **Breech presentation** | **Hypertension, preeclampsia, IUGR** | **Twin pregnancy** |
| Weeks 38-40 | 12 | 9.73 | 10 | 8.06 | 5 | 4.1 | 3 | 2.4 |
| Weeks 34-37 | 27 | 21.7 | 21 | 6.9 | 4 | 3.2 | 2 | 1.6 |
| Weeks 30-33 | 13 | 10.4 | 11 | 8.8 | 4 | 3.2 | 4 | 3.2 |
| Weeks 26-29 | 3 | 2.4 | 2 | 1.6 | 3 | 2.4 | – | – |
under newborn unit because of respiratory problems. All of the cases were discharged from newborn unit postpartum 3rd day in good health. Perinatal morbidity was detected as 13%. There was no perinatal mortality observed.

**Discussion**

Vaginal birth after cesarean is a practicable process for the available selected cases that the risk evaluation is done. Nevertheless, it is still discusses that which birth type is safe for the newborn and whether the vaginal birth after cesarean (SSVD) is an acceptable risk.

As a result of recently studies, the dramatically increase in the ratio of cesarean sections states that it is not a right strategy to make elective second cesarean for every case. Flamm et al states that the maternal mortality is lower in the cases of vaginal birth after cesarean. In addition, maternal complications resulting from surgery such as infection, hemorrhage, injury to internal organs, transfusion needs will be less frequently met and the period of hospital stay will shorten.

It is noted that in the first cesarean induction; when SSVD is tried in the cases having cephalo-pelvic disproportion and/or abnormal labor progress in the event of induction apply, the chance of success decreases. On the other hand, Zelop et al state that the chance of success for vaginal birth after cesarean increases if the estimated fetal weight is below 4000 g.

The most important catastrophic consequence of the SSVD is uterine rupture and the perinatal and maternal mortality and mortality resulting from that. The ratio of perinatal morality is declared as 3.5% and the ratio of perinatal morbidity is declared as 12% in the literature. In our study, perinatal mobility is not seen, and perinatal morbidity is 13% compatible with the literature.

In some studies of the literature, rupture ratios are stated between 0.8% and 1.5%. In our serial, rupture ratio is 2.4% being higher than the literature ratio. There are many studies evaluating the factors increasing the rupture risk in the literature, Bujold et al stated that the rupture risks is 2-3 times more for the cases whose interval between the two pregnancies is shorter than 24 months. In this study, both two cases developing ruptures had intervals between two pregnancies less than 20 months. To summarize, risk factors for uterine ruptures are: cesareans practiced by cephalo-pelvic disproportion inductions, lower vertical cesarean scar, macrocosmic fetus, advanced maternal age and probably the most important one the short interval between two pregnancies. Correlation between the increase in the birth weight and rupture frequency is parallel to the literature. In our study complete rupture was in a case practicing 3820 g SSVD. It is stated that mother’s age being over 30 is concerned with the increase of uterus rupture risk by 2.7 times. Ages of the patients in our working group were between 21 and 40. But we did not detect this kind of complications for the cases over 30 years old. This consequence is similar to the studies of Çalışkan et al.

Developments in trial of labor should be closely followed and evaluated besides estimated fetal weight by ultrasonography in our birth medicine practice. In addition, uterine scar ultrasonography is a helpful method in order to determine the uterine rupture before the birth. Rozenberg et al stated that the risk of uterine rupture and scar partition is low if the bottom segments are thick. Negative predictive value of the uterine bottom segment thickness determined less than 3.5 mm by ultrasonographically detection is denoted as 99.3%.

If deletion or divergence stops during the dissertation following for 2 hours or more, with the cesarean sections of these cases, cesarean ratios increase by 7.9%, and the development of uterine rupture frequency decreases by 42.1%.

There are two applicable examination tools to estimate the success probability of the vaginal birth after cesarean. There are; the scoring system developed by Flamm et al including the parameters of age, previous vaginal birth history, first cesarean induction, cervical partiality and deletion rates and
scoring system developed by Troyer including similar parameters.8,15

As a consequence of this study, starting from the reality that primary cesarean ratios can be decreased by using real inductions, vaginal birth after cesarean is an applicable and acceptable method for carefully selected cases in tertiary reference clinics having adequate supplies and care conditions for the mother and newborn by taking the acceptance of the family.

References
Retrospective Analysis of Multiple Pregnancies

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²Clinics of Gynecology and Obstetrics, Haseki Hospital, Istanbul

Abstract

Objective: To evaluate the multiple pregnancies who had delivered in our clinics retrospectively.

Methods: Two hundred eighty three multiple pregnancies delivered were evaluated retrospectively between January 1999 and December 2004 at Obstetrics Department. The demographic characteristics, maternal age, parity, chorionicity, gestational weeks at delivery, presentation modes of fetuses, delivery modes, neonatal weight, fetal anomaly rate, cesarean rates and indications, perinatal morbidity and mortality rates were evaluated. Statistical analysis were evaluated with SPSS 10.0 S program.

Results: 7674 deliveries occurred in our clinic. 261 (3.4%) twin pregnancy and, 22 (0.29%) triplet pregnancy were found. Dichorionicity was 69.3% and monochorionicity was 30.7% in twin pregnancies. Cesarean section rate was 62.1% in twin and 68.2% in triplet pregnancies. Preterm labour was 23% and preeclampsia was 15.7% in twin pregnancies. Preterm labour was 30%, preeclampsia was 8% in triplet pregnancies. Fetal anomaly rate was 3.6%.

Conclusion: The prevalence of multiple pregnancies has increased because of ovulation induction and assisted reproductive technologies. Professionals should prevent multiple pregnancies due to increased maternal and fetal mortality and morbidity.

Keywords: Multiple pregnancy, chorionicity.

Çoğul gebeliklerin retrospektif analizi

Amaç: Kliniğimizde doğum gerçekleşen çoğul gebelik oğullarının retrospektif analizini yapmaktır.


Bulgular: Kliniğimizde 7674 doğum gerçekleşmiştir. Tüm doğumlar içerisinde 261 (%3.4) ikiz ve 22 (%0.29) üçüz çoğul gebelik oğunu saptandı. Çoğul gebeliklerin 261’ini (%92.2) ikiz gebeliklerin oluşturduğu saptandı. İkiz oğullarının%69.3’ü dikoryonik,%30.7’sinin monokoryonik olduğu saptandı. İkiz gebeliklerinin%62.1’si ve üçüz gebeliklerinin%68.2’si sezaryen ile olmuştur. İkiz gebeliklerin%23’ünde erken doğum eylemi,%15.7’sinde preeklampsı üçüz gebeliklerde ise%30’unda erken doğum eylemi,%8’inde preeklampsı saptandı. Konjenital anomalili oran%3.6 olarak saptandı.

Sonuç: Son yıllarda yardımcı üreme tekniklerinin yaygınlaşması ile birlikte artan çoğul gebelikler beraberinde maternal ve fetal morbidity ve mortaliteye neden olmaktadır. Bu nedenle yardımcı üreme teknikleri ile uğraşan profesyoneller çoğul gebelikleri engellemelidir.

Anahtar Sözcükl: Çoğul gebelik, koryonisite.

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Introduction

There has been a significant increase in the incidence of multifetal pregnancies with widespread usage of ovulation induction assisted reproductive techniques and rate of multifetal pregnancies reached to 3% in recent years. Followings and management of these pregnancies become important because multifetal pregnancies are related to increased maternal and perinatal morbidity and mortality. Most frequent causes of high perinatal morbidity and mortality in multifetal pregnancies are difficult labour caused by presentation abnormalities, respiratory distress syndrome caused by low birth weight and prematurity. Widespread usage of electronic fetal monitorization, obstetrical ultrasonography and improvement of neonatal units ensured progresses in reducing of neonatal morbidity.

Aim of this study is to make retrospective analysis of multifetal pregnancies delivered in our clinic.

Methods

A sum of 283 (3.69%) multifetal pregnancy cases including 261 twin (3.4%) and 22 triple (0.29%) births among a total of 7674 births occurred in our clinic from January 1999 to December 2004 were investigated retrospectively. Ages, parity and chorionicity, pregnancy weeks at the moment of delivery, presentation form of fetus, delivery moods, birth weights, congenital anomaly rate, indication of cesarean section, perinatal morbidity and mortality rates of the cases were examined. It is stated that chorionicity of cases is determined by examination with prepartum ultrasonography and examination of placenta macroscopically after birth. Being more than 15% weight difference among fetuses is described as discordance. SSPS 10.0 S package program is used for statistical evaluation.

Results

261 (92.2%) of multifetal pregnancies were twin. It is found average ages of cases as 28.54 (16-47), gravidas 3.30, parities 2.00. 187 (66.07%) of multifetal pregnancy cases were multipares. It is determined that 10.25% of multifetal pregnancy cases were constituted of pregnant conceived by ovulation induction because of infertility or in vitro fertilization and embryo transfer (IVF-ET). Ratios of twin and triple pregnancies are found as 261 (3.4%) and 22 (0.29%) consecutively among total deliveries in our clinic.

Average pregnancy weeks at the moment of delivery is determined as 33±0.2 weeks in twin and 32±0.7 weeks in triple pregnancies. It is determined that in 85.9% of twin cases birth occurred before 37. week and most frequently between 33-36 weeks and in 90.90% of triple pregnancies gave birth before 37 week and most frequently between 33-36 weeks.

It is determined that 69.3% of twin cases were dichorionic, 30.7% were mono chorionic. It is determined that presentation of twin pregnancies at birth was 38% vertex-vertex, 26.8% vertex-nonvertex, 14.9% nonvertex-vertex, 20.3% nonvertex-nonvertex (Table 1).

According to the mood of delivery 62.1% of twin pregnancies were given birth by cesarean section and 37.9% by vaginally. The most frequent cesarean section indication of twin pregnancies were buttock presentation of before coming fetus (27.8%) and transvers presentation (16%). It is determined that 68.2% of triple pregnancies were given birth by cesarean section and 31.8% by vaginally. It is determined that 45.5% of triple pregnancies were the pregnancies resulted from infertility treatment. The most frequent cesarean section indication of triple pregnancies was also elective (Table 2).

It is determined that average weight of first newborn was 2065±02 g and second newborn was 1972±64 g in twin pregnancies; 1600±45 g, 1648±64 g, 1643±63 g consecutively in triple pregnancies. Furthermore, 63.3% premature birth and 10.6% stillbirth is determined in multifetal pregnancies (Table 3).
It is determined preterm delivery in 23%, premature membrane rupture in 8.8%, placenta insertion anomaly in 1.9%, preeclampsia in 15.7%, HELLP syndrome in 1.9%, intrauterine fetal death in 2.3%, polyhydramniosis in 3.4%, gestational diabetes in 0.8% and heart disease in 0.8% of the twin pregnancies. It is determined preterm delivery in 30%, preeclampsia in 8%, eclampsia in 1%, early membrane rupture in 11% of triple pregnancies (Table 4).

**Table 2. Cesarean section indications in twin pregnancies.**

<table>
<thead>
<tr>
<th>Indications</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breech presentation</td>
<td>45</td>
<td>27.8</td>
</tr>
<tr>
<td>Transvers presentation</td>
<td>26</td>
<td>16.0</td>
</tr>
<tr>
<td>Elective</td>
<td>24</td>
<td>14.8</td>
</tr>
<tr>
<td>Repeated cesarean sectio</td>
<td>22</td>
<td>13.6</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>15</td>
<td>9.2</td>
</tr>
<tr>
<td>Entanglement of umbilical cord</td>
<td>7</td>
<td>4.3</td>
</tr>
<tr>
<td>Arrest of labour</td>
<td>6</td>
<td>3.7</td>
</tr>
<tr>
<td>Fooding breech presentation</td>
<td>5</td>
<td>3.1</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>Arm prolapse</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>Advanced maternal age</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>Face presentation</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Detachment</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Conjoined twin</td>
<td>1</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Table 3. Fetal problems determined in multifetal pregnancies.**

<table>
<thead>
<tr>
<th>Fetal problems</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature birth</td>
<td>119</td>
<td>63.3</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>20</td>
<td>10.6</td>
</tr>
<tr>
<td>Intrauterine dead fetus</td>
<td>6</td>
<td>3.2</td>
</tr>
<tr>
<td>Twin-to-twin transfusion syndrome</td>
<td>6</td>
<td>3.2</td>
</tr>
<tr>
<td>Intrauterine development retardness</td>
<td>17</td>
<td>9.1</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>20</td>
<td>10.6</td>
</tr>
</tbody>
</table>

It is determined preterm delivery in 23%, premature membrane rupture in 8.8%, placenta insertion anomaly in 1.9%, preeclampsia in 15.7%, HELLP syndrome in 1.9%, intrauterine fetal death in 2.3%, polyhydramniosis in 3.4%, gestational diabetes in 0.8% and heart disease in 0.8% of the twin pregnancies. It is determined preterm delivery in 30%, preeclampsia in 8%, eclampsia in 1%, early membrane rupture in 11% of triple pregnancies (Table 4).

Congenital anomaly rate is determined as 3.6% (n=21). Among these congenital anomalies; 28.6% hydrops (n=6), 23.8% neural system anomaly (n=5), 23.8% genitourinary tract anomaly (n=5), 14.2% extremity anomaly (n=5), 4.8% teratoma (n=1), 4.8% conjoined twins (n=1) were determined.

It is determined that discordance ratio was 25% in twin pregnancies and 54% in triple pregnancies. Perinatal mortality rate is determined as 23% (9.2% in twins, 24% in triples) in multifetal pregnancies and 12.6% of them were intrauterine mort fetal.

**Table 4. Obstetrical problems in multifetal pregnancies.**

<table>
<thead>
<tr>
<th>Obstetrical problems</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth</td>
<td>69</td>
<td>41.1</td>
</tr>
<tr>
<td>Premature membrane rupture</td>
<td>24</td>
<td>14.3</td>
</tr>
<tr>
<td>Polyhydramniosis</td>
<td>10</td>
<td>6.0</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>41</td>
<td>24.4</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>5</td>
<td>2.9</td>
</tr>
<tr>
<td>HELLP syndrome</td>
<td>5</td>
<td>2.9</td>
</tr>
<tr>
<td>Placental detachment</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Heart disease</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>4</td>
<td>2.4</td>
</tr>
<tr>
<td>Postpartum atonic bleeding</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Postpartum pulmonary embolism</td>
<td>1</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Discussion**

Multifetal pregnancy rates showed an increase parallel to the widespread usage of assisted reproductive techniques in recent years. In western communities multifetal pregnancies constitutes 3% of pregnancies. It is understood that ratios are approaching these values also in our country. It is found that twin rates reached to 25-30%, triple rates to 5% and pregnancies with more fetus are to 0.5-1%. In our study, it is determined twin pregnancy rate was 3.4%, triple pregnancy was 0.24% and 10.25% of multifetal pregnancies were treatment pregnancies.

As fetus number increases pregnancy period gets shorter. Approximately half of twins deliveries at 36th week or earlier. Average birth week of triple pregnancies was 33.5 week and 90% of them delivers before 37th week, 24% before 32nd and 8% before 28th week. In our study, it is determined 85.9% of twin cases are given birth before 37th pregnancy week. It is determined also 90.9% of triple cases are given birth before 37th and 45.5% before 32nd week. Most of our cases did not take antenatal care and admitted to hospital in late stage of birth. Because of these reasons and also with presence of cases requiring delivery induction like preeclampsia, eclampsia and HELLP syndrome in high proportion, it caused our ratios got higher.

Vertex-vertex presentation is most seen in twins. Usual approach in vertex-vertex presentation cases is birth via normal vaginal tract and cesarean section indications are like in single pregnancies. In our cases vertex-vertex presentation
rate is determined as 58.6% and also it is determined 50.5% of them is given birth via normal vaginal tract and 49.5% of them with cesarean section. It is specified that birth with cesarean section is safer in nonvertex-vertex, nonvertex-nonvertex presentation cases. It is known that fetal mortality is high in locked twin cases. It is determined that before coming fetus was nonvertex in 35.2% of our cases and 93.5% of these cases were given birth by cesarean section. It is preferred birth has to be performed with cesarean section in nonvertex presentation of before coming fetus in multifetal pregnancies in our clinic. Cesarean section rate is reported as 16-44% in twins. In our study, cesarean section ratio of twin cases was 62.1% and it is higher than literature. It grows out of because of our high ratio of nonvertex presentation of before coming fetus, our high ratio of complicated pregnancies and preference of elective cesarean section in treatment pregnancies.

In the study of Buyru et al, they found perinatal mortality rate in newborn given birth by cesarean section lower than given birth via vaginal tract and emphasized that presentation form does not effect mortality directly. In our study, it is determined that in 8 cases (5%) of births by cesarean section and in 17 cases (17.2%), babies with 0-0 Apgar score were given birth. It is determined 60.2% of 118 cases that mortality seen in one week early perinatal period is given birth by vaginal tract and 39.8% by cesarean section. We assessed the higher fetal mortality rate in group given birth by vaginal tract to intrauterine dead fetuses, fetuses with congenital anomalies and immature fetuses are given birth mostly by vaginal tract.

Perinatal mortality is found 4 times higher in twin pregnancies compared to single pregnancies but, there are also studies suggesting there is no difference. Kilpatrick and his friends found the perinatal mortality rates in single pregnancies as 0.25% and in twin pregnancies as 0.11% which has a gestation age above 30 weeks. In our study, perinatal mortality in multifetal pregnancies is determined as 0.16%. Average birth weights of babies constituting perinatal mortality was 1085 grams in twins, 1051 grams in triples; average pregnancy weeks was 28 weeks in twins, 27 weeks in triples. There is statistical significance between perinatal mortality with pregnancy week and low birth weight (p<0.001).

Major malformations occur in 2% and minor malformations occur in 4% of twins. In our study, congenital anomaly ratio is determined as 3.6% and it is compatible with the literature. Furthermore, it is not different from our clinic’s general congenital anomaly ratio of 3.06%. Incidence of transfusion syndrome from twin to twin is not definite but, one fourth of monochorionic twins shows some characteristics of that syndrome. Twin to twin transfusion syndrome is determined in six of our cases and perinatal mortality is determined in these cases except two fetuses. Tan and his friends reported the conjoined twin ratio as 1/60,000. In our study, conjoined twin is determined in one of our case (1/7674) and both of fetuses that delivered by cesarean section became ex at postoperative 36th hour.

Discordance among birth weights in triple pregnancies is three times higher than in twin pregnancies and is a criteria of worst prognose. In our study, discordance among birth weights of fetuses is determined 25% in twins and 54% in triples.

In multifetal pregnancies; it is seen an increase in obstetric complications such as premature birth, early membrane rupture, pregnancy anemia, pregnancy toxicosis, congenital anomalies, abortus, antepartum, intrapartum and postpartum bleedings. The most frequently seen obstetric problems in our cases are determined as preterm birth 41.1%, early membrane rupture 14.3%, pregnancy toxicosis (preeclampsia, eclampsia, HELLP) 30.2% and other complications 14.4%. Coonrad et al reported that preeclampsia is seen four times higher in twin pregnancies compared to single pregnancies. Mastrobatista et al reported that severe preeclampsia is seen as 23% in triple pregnancies and 5% in twin pregnancies. In our study, preeclampsia ratio is determined 15.7% in twin pregnancies as it is determined 9.09% in triple pregnancies.

Increasing in the multifetal pregnancies, as a result of becoming of assisted reproductive techniques widespread, is causing preterm birth, prematurity, early membrane rupture, low birth weight, intrauterine development retardation and
fetal anomalies and also increase in number of individuals with anomalies in further life. Considerable financial sources are spent for newborn care as a consequent of multifetal pregnancies. We consider that preferring single pregnancies instead of multifetal pregnancies will be an appropriate choice to reduce the maternal and fetal morbidity and mortality caused by multifetal pregnancies and also to prevent the financial losses.

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The Predictive Value of Middle Cerebral Artery Peak Systolic Velocity in Repeated Intrauterine Transfusion: A Case Report

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Abstract

Objective: Middle cerebral artery peak systolic velocity has been used for predicting fetal anemia and timing for first and second cordocentesis. However, predicting value of middle cerebral artery peak systolic velocity after multiple intrauterine transfusions is unknown.

Case: Thirty-one-year-old woman, gravida 5, para 4, with Rh-isoimmunization who were presented with fetal hydrops at her 24th week’s of gestation was undergone intrauterine transfusion four times between 24 and 31 weeks of gestation. Doppler examination of middle cerebral artery peak systolic velocity was performed before and after cordocentesis during each procedure. There was an inverse correlation between fetal hemoglobin values and Doppler measurements of middle cerebral artery.

Result: The timing of intrauterine transfusion is traditionally determined by fetal hemoglobin measurement from cord blood of the fetus. Middle cerebral artery peak systolic velocity has been found useful for determining fetal hemoglobin level in the severely anemic fetuses after first and second transfusion. It may also be an appropriate non-invasive alternative in repeated transfusions for the timing of transfusion.

Keywords: Rh-isoimmunization, middle cerebral artery, peak systolic velocity, intrauterine transfusion, severe anemia.

Tekrarlayan intrauterin transfüzyonlarda orta beyin arter tepe sistolik hızının değeri: Bir olgu sunumu

Amaç: Orta beyin arter tepe sistolik hızı, fetal anemi tahmininde ve ilk ve ikinci kordosentezlerin zamanlanmasında kullanılmaktadır. Ancak, tekrarlayan çoklu intrauterin transfüzyonlar sonrasında, orta beyin arter tepe sistolik hızının belirleyici değeri bilinmemektedir.


Sonuç: Tekrarlayan intrauterine transfüzyonlardan, transfüzyonun zamanlanması invaziv bir girişim olan kordosentez ile fetal hemoglobin tayini yapılarak belirlenmektedir. Daha önce transfüzyon yapılmamış ya da tek transfüzyon yapılmış olgularda, fetal anemi tayininde faydalı bulunan orta beyin arter tepe sistolik hızı, çoklu transfüzyonlarda intrauterin transfüzyonun zamanlanması invaziv olmayan uygun bir alternatif olabilir.

Anahtar kelimeler: Rh-izoimmünizasyon, orta beyin arteri, tepe sistolik hızı, intrauterin transfüzyon, ağır anemi.
Background

The Doppler ultrasound and middle cerebral artery peak systolic velocity (OBA-TH) are used in the diagnosis of the fetal anemia ancillary to Rh-isoimmunization as a non-invasive diagnosis method. It has been shown that if according to week of gestation 1.5 folds above the median OBA-TH measurement (1.5 MoM) is used as the threshold value, anemic fetuses at medium or heavy degree can be detected correctly.\(^1\) The method traditionally used to predict which fetus is anemic enough to require transfusion is the cordocentesis and hemoglobin measurement in fetal blood.\(^2,3\) However, this method has a 1-2% percent risk of fetal loss and at the same time increases the risk of sensitization.\(^4\) In cases which it is necessary to repeat the intrauterine transfusion, the timing of the subsequent transfusion is done according to the hematocrit value derived after the transfusion. OBA-TH has been found useful in determining the degree of fetal anemia and consequently the transfusion requirement in fetuses which were never transfused before or were only transfused once.\(^5\) However, adult red cells which change place with fetal red cells differ in terms of their capacity to carry oxygen, aggregation characteristics and viscosities.\(^5\) As a result, the effect of fetal blood characteristics that change after repeated transfusions on the OBA-TH measurement is not precisely known.

Our objective with this case report is to emphasize the association and significance of OBA-TH measurements with fetal hemoglobin values in a hydropic fetus treated with repeated intrauterine transfusions.

Case

Thirty-one-year old woman, G5, P4, who was referred to Celal Bayar University Department of Obstetrics and Gynecology, Perinatology on her 24\(^{th}\) week of gestation upon the detection of ascite and hydrops in the abdomen of the fetus in the ultrasonography. Epidemic ascite was detected in the abdomen and edema was detected on the scalp and abdominal walls in the ultrasonography (Figure 1). The patient with an obstetric history of gestational loss and fetal mortality due to three Rh-isoimmunizations was found to be negative in the indirect coombs test applied one week prior to contact despite being monitored with the indirect coombs test since the 13\(^{th}\) week of gestation. The patient with the repeated indirect coombs test was notified that the test result is positive and that the antibody titre is too high for titration. Cordocentesis was done one the 24\(^{th}\) week of ges-
tation of the patient for whom intrauterine transfusion was decided. Upon hemoglobin (Hb) values being 3.5 g/dL, hematocrit (Htc) 13%, the 80% hematocrit, 0 Rh (-), serologic infection tests being negative, the amount of blood which is necessary to be given in the previously defined form, through the transperitoneal and intravascular method was calculated with the formula and transfused with the plan to increase hematocrit to 30%. Blood was taken after the transfusion process for the Hb and Htc values, however, these values could not be reviewed due to the technical failure in the laboratory. The fetal blood type 0 Rh (+) was positive with the direct Coombs test. Pre and post transfusion OBA-TH was measured from the peak waveform in way to enable the angle between the Doppler ultrasound and artery to be near 0, in the form previously described with the Doppler ultrasonography (Figure 2). The patient had undergone three more intravascular transfusions up to the 31st week of her gestation. Fetal Hb and Htc values and also OBA-TH measurements were taken before and after the transfusion are all shown in Table 1. On the 2nd transfusion, the decision as to when the transfusion would be repeated was taken due to the continuation of fetal ascite, and according to post transfusion fetal Hb and Htc values in the following transfusions. The fetus was observed between transfusions a couple of times per week with ultrasonography, and in addition, weekly with the non-stress test after the 28th week of gestation. Fetal ascite disappeared after the 2nd transfusion (Figure 3). While fetal Hb and Htc values increased after the transfusions, the measured OBA-TH decreased (Table 1). There was an inverse correlation between the fetal Hb, Htc values and the OBA-TH.

Upon the development of acute persistent bradicardia during the final transfusion performed on the 31st week of gestation, a 1900 gr live baby girl was delivered with an emergency caesarean section. The Hb and Htc value after delivery was 11 g/dL and 34%, relatively.

Discussion

The measurement of OBA-TH with the Doppler ultrasound is a valuable tool in the assay of the
Fetal hemoglobin value in fetuses carrying the risk of anemia. It has been found to be useful in the assay of fetal hemoglobin value and the prediction of the time of transfusion in anemic fetuses with severe or medium degree anemic fetuses even if the value of prediction is not too high in lightly anemic or non-anemic fetuses. In fetal anemia related to Rh-isoimmunization, cardiac “output” increases in response to hematocrit decrease and fetal cerebral arteries increase blood flow with quick response to hypoxia. If OBA-TH values are above 1.5 MoM according to week of gestation, it is considered that the fetus has severe or medium degree of anemia. However, OBA-TH values may show variation since the characteristics of fetal blood change in fetuses that have previously undergone transfusion due to the adult blood given. Thus, when 100% sensitivity is taken in the detection of severe, medium degree and light anemia with studied OBA-TH measurements in the prediction of the 2nd transfusion time for cases which have undergone transfusion for one time, the wrong positive rate has been found to be 6%, 37% and 70%, respectively. Researchers have

**Tablo 1.** Hemoglobin, hematokrit ve OBA-TH’nin transfüzyonlar öncesi ve sonrası değerleri.

<table>
<thead>
<tr>
<th>Transfüzyon No</th>
<th>Gebelik haftası (Aralık)</th>
<th>Hemoglobin</th>
<th>Hematokrit (%)</th>
<th>Verilen kan miktar (ml)</th>
<th>OBA-TH (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Germans</td>
<td>Hindi</td>
<td>Javan</td>
<td>Norwegian</td>
<td>OBA-TH (cm/s)</td>
</tr>
<tr>
<td>1</td>
<td>24. hafta (10 gün)</td>
<td>3.5 – –</td>
<td>11.5 – –</td>
<td>40 – –</td>
<td>52 – (1.7 MoM)</td>
</tr>
<tr>
<td>2</td>
<td>25. hafta (16 gün)</td>
<td>1.5 – 8.9</td>
<td>3 – 27</td>
<td>75 – 80</td>
<td>39 – (&gt;2 MoM)</td>
</tr>
<tr>
<td>3</td>
<td>27. hafta (21 gün)</td>
<td>5.9 – 10.2</td>
<td>17.8 – 29.4</td>
<td>55 – 50</td>
<td>27 – (1.3-1.5 MoM)</td>
</tr>
<tr>
<td>4</td>
<td>31. hafta</td>
<td>5.7 – 11</td>
<td>17 – 34</td>
<td>60 – 0.63</td>
<td>* – (1.5 MoM)</td>
</tr>
</tbody>
</table>

*Acil sezaryen ihtiyaç nedeniyle ölçemedi.*

**Resim 3.** Transfüzyon sonrası azalan asit.
reported the OBA-TH threshold value for severe anemia in the same study as 1.69 MoM. This value is higher than the threshold value for cases that have not undergone any transfusion before (1.5 MoM). The low capacity to carry oxygen and low viscosity of the “new” blood has been indicated as the cause of this. There is no study in relation to the OBA-TH value in determining the fetal anemia in intrauterine transfusions repeated more than once. Furthermore, it is suggested that the measurement of OBA-TH with the Doppler ultrasound particularly in hydric fetuses could be an ancillary method in determining the fetal hemoglobin value with cordocentesis and amniocentesis, however that it cannot substitute these methods.

In our case, the OBA-TH measured before the first transfusion when the fetus was in the hydropic state was over the 1.69 threshold value. The OBA-TH value which dropped below 1.5 MoM after the transfusion increased again over 2 MoM in 10 days after the first transfusion. These values were inversely proportioned with the fetal Hb and Htk values measured with cordocentesis. However, despite the OBA-TH values measured after the 2nd transfusion being below the threshold value necessary for transfusion, the Hb and Htc values observed with cordocentesis were at the border requiring transfusion (Table 1). These values indicate that it may be necessary to use different threshold values from fetuses that have not undergone transfusion before or that have undergone transfusion once only for OBA-TH measurement and fetal hemoglobin assay in transfusions repeated more than once in hydric fetuses. However, since it will not be possible to reach a conclusion with a single case, new prospective studies are necessary to predict the OBA-TH value and threshold values in fetal hemoglobin assay in repeated transfusions. The objective of this case report is not to reach a conclusion on this subject, but to emphasize this requirement.

A majority of the cases with Rh-isoimmunization are non-anemic or are lightly anemic. In their study, Detti et al. report the ratio of non-anemic or light anemic fetuses as 72%, medium degree anemic fetuses as 11%, and severely anemic ones as 17%. The low proportion of pregnant women who are severely anemic and far from their term makes it difficult to reach the sufficient number of cases in a prospective study on the subject.

In our case, post transfusion fetal Hb and Htk values dropped quicker than expected. The cause of this may be high maternal antibody titre or the intraperitoneal application of a section of the first transfusion. It is suggested that red cells given intraperitoneal are absorbed later in hydric fetuses and consequently, intravascular transfusion is preferred. On the other hand, some authorities recommend the intravascular and intraperitoneal method in combination, and suggest that red cells that are to be left for the peritoneal will form a reservoir. For this reason, in the first transfusion we preferred to combine the intraperitoneal method with the intravascular one. As a result, OBA-TH which is found to be useful in the assay of fetal anemia in cases that have not undergone any transfusion before or that have undergone a single transfusion, may be a suitable non-invasive alternative in the timing of the intrauterine transfusion in multiple transfusions. There is need for prospective studies on this subject.

References


Objectives: Twin pregnancies are the pregnancies that intrauterine and perinatal morbidity and mortality is higher when compared to monozygotic pregnancies.

Cases: 10% of all perinatal deaths are related with dizygotic twins. In this study we reported four twin pregnancies that had intrauterine death of one twin at 20th week or later. We analyzed the cases according to maternal age, ultrasonographic findings, results of biochemical tests, birth weeks and perinatal outcomes. One case was monochorionic - monoamniotic and the other three were dichorionic - diamniotic. In two cases other twins died at 9th and 13th days after the diagnosis. The other two that were dichorionic - diamniotic reached term without any complications.

Conclusion: In case of monofetal death of twin pregnancies, the type of placenta should be analyzed and then follow up and treatment modalities of these cases should be chosen.

Keywords: Twin pregnancy, single fetal death.

Background

Twin pregnancies are the pregnancies that intrauterine and perinatal morbidity and mortality is higher when compared to monozygotic pregnancies. In multiple pregnancies, the frequency of complications including preterm birth, preeclamps-
sia, intrauterine growth retardation, and twin-to-twin transfusion syndrome is increased.\(^2,3\) 10% of all perinatal deaths are related with dizygotic twins. The rate of intrauterine fetal demise in multiple pregnancies is higher three times of monozygotic pregnancies. Perinatal morbidity and mortality are seen in dizygotic pregnancies frequently three times to monozygotic pregnancies.\(^1\)

The demise of one of the twins in first trimester is relatively seen in general and it doesn't harm the mother and the other fetus in following weeks and doesn't affect the maternal prognosis.\(^4,5\) However, the demise of one of the twins may cause serious problems for both mother and the fetus in second or third trimester.\(^6\) Major maternal and another fetal problems are intravenous coagulation, neurological and nephrologic damage, premature birth.

In this case study four twin pregnancies that had intrauterine death of one twin at 20th week or later are diagnosed and discussed. Four twin fetuses are diagnosed in 20th week or later intrauterine exitus. The cases were analyzed in regard the age, pregnancy, ultrasonic findings, biochemical tests, maternal weeks, and perinatal results.

**Case**

Four twin fetuses which are monitored within Perinatology Unit of SSK Ege Maternity and Gynecology Training Hospital, are diagnosed in 20th week or later intrauterine exitus. The cases were analyzed in regard the age, pregnancy, ultrasonic findings, biochemical tests, maternal weeks, and perinatal results.

In four cases constituting research group, both fetuses were alive, proven by the first trimester ultrasonography. Average maternal age of four cases was 27 (between 23-31). Pregnancy week average where one of the twin fetuses was demised 24 (between 20-28th weeks). Ultrasonographic tests showed that one case was monochorionic monoaomiotic and the other three cases are dichorionic diamniotic. The other fetus was demised 13 days later once monochorionic monoaomiotic case twin was exitus. In another case, the other fetus was exitus 9 days later than the first one. In other two cases that reach the term, pregnancy week average was 37 weeks and 3 days (between 37-38th weeks). Prenatal ultrasonographic monitoring was consistent with the latest tests and biophysical profiles were normal. In Doppler blood flow tests, umbilical artery, uterine artery and middle cerebral artery flow patterns were in normal limits. Average values of the current blood analysis for 4 cases: fibrinogen; 224 (193-248 mg/dl), prothrombin time; 13.4 second (12.1-14.8 second), thrombocyte counts; 166.000/mm\(^3\) (119.000-209.000 trombosit/mm\(^3\)), hemoglobin; 12.8 g/dl (14.2-11.6 g/l), leukocyte; 11.250/mm\(^3\), FDP (Fibrin decomposition products); 1.000 ng/dl. All four cases were monitored during their hospitalization and two of them were monitored on monthly basis by ultrasonography and laboratory tests. In two cases where the twin fetuses were intrauterine demised and pregnancies terminated by inducing by misoprostol abortion. These cases were discharged without any complication on the first day of postpartum. In the other two cases that reach the term, delivered by cesarean. In one case, a male fetus with 3000 g weight and 9 Apgar, and a male exitus fetus with 1400 g, in the second case a male fetus with 3000 g weight and 7 Apgar, and a male exitus fetus with 700 g weight were delivered. No neonatal morbidity has been diagnosed for both fetuses. Mothers were discharged without any complication on the second day of postoperative period. Macroscopic placenta examinations and ultrasonographic monitoring in postpartum period showed that one of the cases was monochorionic monoaomiotic and the other three were dichorionic diamniotic. As per fetal mortality etiology, the ultrasonographic monitoring in the monochorionic monoaomiotic case, as there was oligohydranmios in demised fetus, and polyhydramnios, acid, hydrops findings in other case, Twin-to-Twin transfusion was planned, the exact etiology couldn't be clarified in other three diamniotic dichorionic cases.

**Discussion**

The mortality through the exitus of one twin, and major morbidity rate was reported 46%.
Though the etiology cannot be strictly detected in numerous cases; twin-to-twin transfusion syndrome, preeclampsia, rhesus immunization, chromosomal or congenital anomalies, single umbilical artery, placental and umbilical cord placement anomalies, umbilical venous thrombosis and uterine malformations are major causes. As the etiology of fetal mortality in our cases, by the ultrasonographic monitoring in the monochorionic monoamniotic case, as there was oligohydramnios in demised fetus, and polihydramnios, ascites, hydrops findings in other case, twin-to-twin transfusion syndrome was decided; the exact etiology couldn’t be clarified in other three diamniotic dichorionic cases.

Major factors determining the treatment and follow-up approach in multiple pregnancies complicated with intrauterine monofetal death are the risks that mother and living fetus take. Most frequently used and suggested method is follow-up of the maternal coagulation system by a series of lab test. Pitchard et al proved that there is coagulation disorder at various levels in mono pregnancies left in uterus after the exitus. When one of the twins dies, the pregnancy is terminated by cesarean because of the coagulopathy development and this increases the prematurity related morbidity.9 In our study, the lab test results for coagulation system were within the normal limits.

There are various studies that indicate that the living fetus is under high morbidity and mortality risk. After the first fetus demised, there is an intrauterine mortality risk at 7.8 - 20% for living fetus.14 In addition, in 28-50% of live-born fetuses, central neural system damage at various levels occur.5 The amount of blood transfused to demised fetus from the living one, the type, the density and the placement of the anastomosis in monochorionic placenta, and this determines the anemia and organ damage in living fetus. No complication has been developed in the living fetuses that complete the term.

In monochorionic monoamniotic twin pregnancies, in case where one of the fetuses demises in antenatal period, termination of the pregnancy is preferred.11 However, because the cerebral and nephrologic complications developed in living fetus started once the other fetus demises, a close follow-up is suggested as a conservative treatment.6 But as there is no such a problem in diamniotic dichorionic twin pregnancies, conservative approach is preferred, and ultrasonographic follow-up of the fetus development and amnion fluid is suggested.12 Non stress test and Doppler ultrasonography monitoring are important for detecting fetal distress development, twice in a week.6 In the same time, the maternal coagulation system should be monitored by a series of lab test. Most important factor to determine the mode of delivery is general obstetric situation of the mother. Twin pregnancy and the demise of one fetus cannot constitute indication for the cesarean. When one of the twins dies, the pregnancy is terminated by cesarean because of the coagulopathy development and this increases the prematurity related morbidity.9

In conclusion, in case of monofetal death of twin pregnancies, the amnion and placenta structures should be detected and then follow up and treatment modalities of these cases should be chosen. If placenta and amnion are diamniotic dichorionic, a conservative approach including close follow-up may be adopted until the lung maturation of the fetus is ensured. In cases that term or viability limit are reached, emergency delivery is generally accepted. While determining the birth modality, the obstetric indications should be considered and the prematurity should be avoided.

References


Impetigo Herpetiformis: A Case Report

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Abstract

Objective: Impetigo herpetiformis is a rare and potentially life-threatening pustular dermatosis affecting mainly pregnant women. We report here a case of impetigo herpetiformis which occurred in twenty-ninth week of pregnancy.

Case: A 32 year old gravida 2, para1 pregnant woman who was referred to our institution because of congestive heart failure, gestational diabetes mellitus and oligohidroamnios in 27th gestational age was hospitalized. Eruptive pustular lesions which appeared in 29th week of the gestation has spread her entire body. Her pustular cultures were negative. A punch skin biopsy from a pustule on the trunk made the diagnosis of impetigo herpetiformis. The patient who developed spontaneous uterine contractions was treated with betamethazone and tocolysis. The patient who did not respond to this treatment was taken to delivery at 30 weeks of gestation. The newborn showed no skin lesions after birth. The skin lesions of the mother improved in the second postpartum week.

Conclusion: The rates of maternal mortality and fetal mortality and morbidity due to placental insufficiency are increased in impetigo herpetiformis. To reduce the mortality and morbidity rates the antenatal management of impetigo herpetiformis should be organized with a multidisciplinary approach.

Keywords: Impetigo herpetiformis, generalized pustular psoriasis.

Impetigo herpetiformis: Bir olgu sunumu


Sonuç: Impetigo herpetiformis olgularında maternal mortalite, ayrıca fetoplazental yetmezlik nedeniyle fetal mortalite ve morbidiye oranları artmıştır. Bu oranlar azaltılım için antenatal işlem protokollerini multidisipliner bir yaklaşımla düzenlemek gerekktedir.

Anahtar kelimeler: Impetigo herpetiformis, jeneralize püštüler psoriasis.

Background

Impetigo herpetiformis is a rare and potentially life-threatening pustular dermatosis affecting mainly pregnant women. The disease was triggered by hormonal disorder in pregnancy. It has various clinic and histological similarities to the generalized pustular psoriasis. Impetigo herpetiformis is considered as variant of pustular psoriasis that appears in pregnancy.
In the literature more than 100 cases were described. Fetal mortality and morbidity risks are high because of maternal mortality and placental deficiency. This case report was presented in order to highlight the importance of impetigo herpetiformis in maternal and fetal mortality and morbidity. Although it was seen among 6-33 age group, it was also reported for menopause group.

Case

Mrs. AT is 32-year-old. In 27th gestational week, she was referred to our clinic with 2 para 1 congestive heart failure, oligohydramnios diagnosis. She had diagnosed mitral stenosis, and tricuspid failure and used digoxin. The patient delivered a spontaneous vaginal unvivid birth 1 year earlier when an in utero fetal loss has been developed in her first pregnancy. She is hospitalized once she has atrial fibrillation and gestational diabetes on 27th week of current pregnancy.

In ultrasonographic monitoring, fetal biometry was consistent with latest monitoring. In Doppler measurement, dicrotic notch was monitored in bilateral arteries, while umbilical artery and middle cerebral artery were normal. The treatment arranged by regular insulin, digoxin, diltizem, acetyl salicylic acid, low molecule weight heparin.

On 29th gestational week, skin lesions appeared in the pubical zone, with itchy, eritematous (Figure 1). The periphery pustules were spread to all over the body (Figure 2). Oral mucosa and soft palate 2-3 mm eritemous papules were developed. The hair with hair, plamar-plantar surfaces and fingernails were intact.

Laboratory results, leukocyte 14000/mm³, erythrocyte sedimentation rate (ESR): 29 mm/h, serum calcium: 7.3 mg/dl, serum phosphate: 2.5 mg/dl, albumin: 2.41 gr/ml. Liver, kidney function tests and parathyroid hormone levels were normal.

There was no bacteriologic reproduction in the specimens acquired from pustule and in blood culture. The histological examination of biopsy material taken from the lesion displayed that multilocular spngy intraepidermal pustules, acanthosis, parakeratosis (Figure 3).

The case was diagnosed Impetigo herpetiformis based on the clinical and histopathological features. As a result of the dermatological consulta-
tion, local betamethazon administration, 3 times per day, (Betnovate cream, Glaxo Welcome Medical Industries A.S, Istanbul, Turkey) has begun.

On 29th gestational week, in order to stimulate lung maturation and contribute to the treatment of the lesions, betamethazon 12 mg/24 h (Celestone chronodose; Schering Plugh Medical Products AS, Istanbul, Turkey).

In 29th gestational week, the case that developed premature membrane rupture, delivered a male infant, 1450 g, 42 cm, 12 hours later by a vaginal modality. According to Lubchenco–LO maturation curve, the weight was 50 percentile, the length 75 percentile. The skin lesions were ameliorated within 2 weeks post partum.

**Discussion**

Impetigo herpetiformis is a dermatosis characterized by sterile pustules that occur in pregnancy. The disease appears in pregnancy. Some indicates that it has an etiological relationship with the pregnancy. Even though there isn’t any strict pathological mechanism, the use hypocalcaemia, hypoparathyroid, infection, oral contraceptive and stress are known to facilitate the development of impetigo herpetiformis.

It appears in second and third trimesters but mostly occurs in third trimester. The frequency is variable and the symptoms don’t completely ameliorate. In following pregnancies, it tends to appear earlier and acute. In our study, lesions appeared in third trimester.

It may be life-threatening for both mother and fetus. The dermal lesions are intensified sepsis risk, while placental defect and decreasing intervillous circulation may cause fetal morbidity and mortality. Lesions begin with symmetrical eritemous plaques in convolution of the skin. Sterile pustules appear in the periphery of the plaques. The pustules amalgamate and expand to the periphery when the center opens and crust. Oral and pharynx lesions may be developed. General situation worsens and systemic symptoms including lassitude, headache, fever, palpitation, nausea, diarrhea, tetani as well as eruption. In our case, lesions started from pubical zone and expanded to
the body. The lesions are seen in oral mucosa and soft palate tissue. In lesion samples, no bacteriological reproduction has been observed. Further systemic findings haven't been diagnosed in our study. The lesions are ameliorated in postpartum period, leaving a postinflammatory pigmentation, in a couple of weeks. In our case study, the lesions were ameliorated within 2 weeks.

Leukocytosis, hypocalcaemia, hyperphosphatemia, hypoproteinemia, ESR increase are most frequent laboratory findings. It is noted that hypoalbuminemia develops as a result of albumin loss from large exudative zones, and hypocalcaemia appears as a secondary effect of the hypoalbuminemia. In the differential diagnosis of the cases, subcorneal pustular dermatosis may be considered. But, the general situation doesn't corrupt in subcorneal pustular dermatosis. In our case, leukocytosis, hypocalcaemia, hypoalbuminemia, ERT increases were diagnosed. Parathormone levels were normal.

In impetigo herpetiformis cases, as a histopathological symptom in a lesion, polymorphic leukocyte accumulation at epidermis spongious zones, are characteristic, and they are accepted similar to the spongiform pustules of Kogoj specific to the psoriasis. Extension and parakeratosis are frequently monitored. In our case, prolongation in spongiform pustular papillary and parakeratosis have been diagnosed.

Most important complication of the disease is placental defect, and intrauterine fetal mortality. In our case, while impetigo herpetiformis related placental defect develop as well as maternal heart failure related intrauterine maturation latency, gestational diabetes ensured that intrauterine maturation develops in normal limits.

For treatment in less severe cases, topical steroid applies, besides, in severe cases systemic steroid is in use. For secondary infections, antibiotics, fluid, electrolyte and calcium replaced. In hyperparathyroidism cases, phosphate limitation, calciferol and dehydrocolecalciferol applications are suggested. For treatment resistant cases, cyclosporine and phototherapy treatments are in use. In our case, topical steroid wasn't administrated since systemic symptoms haven't been diagnosed. In addition, systemic parenteral corticos-
teroid was administrated in order to stimulate lung maturation. In post partum period, systemic corticosteroid administration wasn’t continued since a diminution was expected in lesions. Parenteral calcium replacement was used.

Since it is similar in clinic and histopathological regard, impetigo herpetiformis may be a variant of the generalized pustular psoriasis. It is similar in clinic and histopathological regard, impetigo herpetiformis may be a variant of the generalized pustular psoriasis.5,6 Impetigo herpetiformis is seen in the persons that don’t have psoriasis in their personal or family history, and it is induced after the birth.5,9 It is known that it repeats in successful gestations, more severe and earlier.5 In our case, it appears the first time in second gestation. The psoriasis wasn’t reported in personal or family history.

The symptoms of the psoriatic cases are reduced at 30-65% when the patients are conceived. The symptoms worsen only in 10-20% of the cases.9 The amelioration occurs generally in first trimester. The gestational response remains the same in following gestations. The amelioration in psoriasis table for the pregnant women is related to the immune system down regulation.10,11 87.7% of the cases are involved after the pregnancy. In our case, lesions are rapidly induced after the gestation. Our case was diagnosed in clinic development as impetigo herpetiformis as it was similar in regard of morphologically and histological appearance. This rare entity is important for both maternal and fetus mortality and morbidity.

References
Treatment of Viable Cesarean Scar Ectopic Pregnancy with Intraamniotic Methotrexate Injection

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Abstract

Objective: Pregnancy in previous cesarean scar is the rarest form of ectopic pregnancy. We aimed to present a case of cesarean scar ectopic pregnancy that was successfully treated with intraamniotic methotrexate injection under ultrasonographic guidance.

Case: A 41-year-old woman, gravida 4, para 2, abortus 1, with a history of two caesarean sections, presented at 5 weeks' gestation and requested pregnancy termination. Upon transvaginal ultrasonography, a hypoechogenic round-shaped mass image, 10x9 mm in diameter - similar to gestational sac - which was localized on Kerr incision, just upon the internal cervical os, was identified. Neither yolk sac nor fetal pole was identified. Serum beta-hCG was 7595 mIU/ml. The patient was re-examined a week later. Transvaginal ultrasonography revealed that the gestational sac diameter proceeded to 24x15 mm with a fetal pole with cardiac activity and beta-hCG was 14000 mIU/ml. Intraamniotic methotrexate (MTX) (10 mg) injection was applied under ultrasonographic guidance. The hemodynamically stable patient was followed on outpatient basis. Serum beta-hCG levels were 20252 mIU/ml and 19399 mIU/ml, with one week intervals. Gestational sac diameter decreased to 15x10 mm with loss of the fetal pole image. Due to the increasing levels of beta-hCG, intraamniotic MTX injection was repeated at a dose of 20 mg, 2 weeks after the first injection. Thereafter, the patient was followed with serial ultrasonography and serum beta-hCG monitoring. Cesarean scar pregnancy was completely resolved upon 9 weeks interval.

Conclusion: Ultrasound-guided methotrexate injection is a successful alternative to terminate cesarean scar pregnancy.

Keywords: Cesarean scar pregnancy, conservative treatment, intraamniotic methotrexate

Canlı sezaryen skar gebeliğinde intraamniotik methotrexat enjeksiyonu ile başarılı tedavi

Amaç: Nadir bir ektopik gebelik türü olan bir sezaryen skar gebelik olgusunun sunulması ile tanı ve tedavi modalitelerinin literatür işığında tartışılması.

Olgu: Kırkbir yaşındaki G4P2A1 olan hastanın 9 yıl ve 3 yıl önce 2 kez sezaryen sekısı ile doğum yaptığı öğrenildi. Bir haftalık adet rötarı bulunan hasta aile planlaması isteği ile kliniğiimize başvurdu. Yapılan transvajinal ultrasonografide (TVUSG) internal os'un hemen üstünde eksantrik yerlesilmiş, Kerr incision hattının üzerinde gestasyonel kese ile uyumu hipoekojen halka şeklinde ve 10x9 mm çapında yapı izlenildi. İçinde yolk sac ve fetal pol izlenmedi. Hastanın beta-hCG düzeyi 7595 mIU/ml olarak geldi. Bir hafta sonra tekrarlanan TVUSG'de gestasyonel kesenin 24x15 mm çapı ulaşığı ve içinde kalp atımı izlenen fetal imge olduğu gözlemdi. Beta-hCG düzeyi 14000 mIU/ml olarak geldi. Hastaya sezaryen skar gebelik tanısı ile TVUSG eşliğinde gestasyonel kese içine, intraamniotik 10 mg methotrexate enjeksiyonu yapıldı. Kanaması olmayan hasta ayaktan takibe alındı. Yapılan takiplerde hastanın beta-hCG düzeyi 1 hafta arı ile 20252 mIU/ml ve 19399 mIU/ml geldi, gestasyonel kese 15x10 mm'ye geriye düşüldü ve betahCG düzeyinin düşmesine-aksine artması nedeniyle, birincı methotrexat enjeksiyonu takiben 2 hafta sonra yeniden TVUSG eşliğindeki ikinci intraamniotik methotrexat enjeksiyonu (20 mg) yapıldı. Beta-hCG taşkını olan hastanın haftalık takiplerinde beta-hCG değerinin düştüğü ve gestasyonel kese görüntüsünün rezorbe olduğu izlenildi.

Sonuç: Son yillarda sezaryen secitio ile yapılan doğumların artması nedeniyle uterin skar gebelikler de daha sık gözlenmeye başlamıştır. Uterin skar gebeliğinin tedavisinde TVUSG eşliğinde intraamniotik methotrexat enjeksiyonu etkin ve başarılı bir yöntemdir.

Anahtar Sözcükler: Sezaryen skar gebelik, konservatif tedavi, intraamniotik methotrexat

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Background

The pregnancy implanted in cesarean scar is the rarest form of the ectopic pregnancy, is a clinical case containing life-threatening situation. Since it is so rare, there isn’t any agreed clinical administration. The data in the literature is mostly formed of the case studies. In English literature, as from 2002, 66 cesarean scar pregnancy cases were reported. This figure reflects increasing cesarean births and the use of transvaginal ultrasonography for diagnosing scar pregnancies. Former cesarean cases, the risk factors for scar pregnancy are dilatation, and curettage history, placental pathology, ectopic pregnancy history and in vitro fertilization cycle. Among the treatment options, there are direct methotrexate or potassium chloride injection and/or systemic methotrexate injection, vaginal sonography, as well as embryo aspiration, spooling treatment, removing the gestational tissue through laparotomy, dilatation and curettage, transarterial uterine artery embolization. However, in the extent of the examined case series, direct methotrexate injection, accompanied by ultrasonic monitoring is the most appropriate option.

We aimed to discuss the diagnosis, treatment, follow up approaches in light of the literature, to emphasize the importance of transvaginal sonography in early diagnosis and follow-up.

Case

A 41-year-old woman, with a history of two caesarean sections, which one was 9 years ago and the other 3 years ago. The patient who has 1 week menstrual latency, requested the hospitalization for abortion. Upon transvaginal ultrasonography, a hypoechogenic round-shaped mass image, 10x9 mm in diameter -similar to gestational sac- which was localized on Kerr incision, just upon the internal cervical ostium, was identified. Neither yolk sac nor fetal pole was identified. Serum beta-hCG was 7595 mIU/ml. The patient was re-examined a week later. Transvaginal ultrasonography revealed that the gestational sac diameter proceeded to 24x15 mm with a fetal pole with cardiac activity and beta-hCG was 14000 mIU/ml. The patient has

Figure 1. Ultrasonographic image of scar pregnancy.
undergone 10 mg methotrexate injection accompanied by TVUSG directly into the uterus upon the cesarean scar pregnancy diagnosis. The patient who hasn't hemorrhage underwent an outpatient follow up. In the monitoring, beta-hCG level was measured 20252 mIU/ml and 19399 mIU/ml, gestational mass was reduced to 15 x 10 mm and fetal image was disappeared. Since Beta-hCG level augments, after first methotrexate injection, within 2 weeks, second intraamniotic methotrexate injection was made (20 mg). After 3 days of second dose methotrexate injection, the patient flood during 10 days. 10th day of the vaginal bleeding, transvaginal ultrasonography was repeated and showed that the diameter of the gestational sac was reduced to 5 x 5 mm and serum beta-hCG level was reduced to 1778 mIU/ml. Serum beta-hCG was 3259 mIU/ml after one week. The vaginal hemorrhage stopped and transvaginal USG showed that the gestational sac was still 5 x 5 mm. Weekly beta-hCG follow up indicated the values and the image of gestational sac disappeared. Figure 1 and 2 show the weekly gestational sac and serum beta-hCG results. Consequently, cesarean scar pregnancy was completely resorbed in the end of 9th week.

**Discussion**

Cesarean scar pregnancy was a contraindication of the cesarean cases that are showing a significant increase in recent years. In a series of 12 cases studied by Seow et al reported that, cesarean scar pregnancy frequency was estimated 1/2226 and scar pregnancy rate was 6.1% for women that have at least one cesarean birth and one ectopic pregnancy. The pregnancy age was 5-12 weeks on diagnosis, and the time between latest cesarean and scar pregnancy was found 6-12 months. To 12 patients, direct methotrexate or potassium chloride injection and/or systemic methotrexate injection, vaginal sonography, as well as embryo aspiration, spooling treatment, removing the gestational tissue through laparotomy, dilatation and curettage methods were applied and 11 of 12 patients retained their reproductive ability. And one patient who had undergone dilatation and curettage had hysterectomy.

![Figure 2. Ultrasonographic image of scar pregnancy.](image-url)
because of excessive bleeding. However, in the extent of the examined case series, direct methotrexate injection, accompanied by ultrasonic monitoring is the most appropriate option and surgical/invasive methods should be avoided because of the high morbidity. Our case is a with a history of two caesarean sections, which one was 9 years ago and the other 3 years ago. The pregnancy age is weeks on the diagnosis. In order to be sure of scar pregnancy, ultrasonography of the patient was repeated 1 week later and showed that the diameter of gestational sac increased and fetal image appeared, beta-hCG was elevated. 10 mg MTX injected to the patient accompanied by transvaginal USG. During the 15 days follow up, despite the fetal image disappeared beta-hCG didn’t reduce, in contrary elevated and through second USG 20 mg MTX injection was applied. Following the second

![Weekly change of GS](image1)

**Figure 1.** Weekly change in diameter of gestational sac (GS).

![Weekly hCG](image2)

**Figure 2.** Weekly serum beta-hCG.
treatment, the scar pregnancy begun to resorb rapidly. Since the scar pregnancy is a rare form of the ectopic pregnancy, treatment schedule is different according to the patient. The data in the literature is mostly formed of the case reports. Based on the presented case, transvaginal USG and serum beta-hCG are important indicators in the follow up of the scar pregnancy treatment. Beta-hCG values that don’t reduce or indifference of ultrasonographic pregnancy image are related to the unsuccessful treatment or readministration of dose. On the other hand, resorption of the scar pregnancy ultrasonographic image, administrated intraamniotic MTX may last 2-12 months.3,7 Researching the literature, 54% of the ectopic pregnancy cases delivered 2 or more cesarean fetus and 30% had dilatation or curettage operation. For the women with ectopic pregnancy, placental pathology (placenta previa) history and the ones with 2 or more cesarean (in particular, because of bottom-down presentation), the scar pregnancy development is more probable.1

In conclusion, cesarean scar pregnancies are frequently observed in recent years as cesarean births are increased. Being aware of this possibility and using early transvaginal USG augment the early diagnosis and the success of the conservative treatment and prevents the surgical operation requirements that may cause hysterectomy.

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