

PERINATAL JOURNAL

Volume 18 / Issue 3 / December 2010

The Official Publication of Turkish Perinatology Society



PERINATAL JOURNAL

Volume **18** / Issue **3** / December **2010**

The Official Publication of Perinatal Medicine Foundation

On behalf of the Perinatal Medicine Foundation: Murat Yayla

Managing Editor: Cihat Şen

www.perinataljournal.com

Editor-in-Chief

Cihat Şen

Associate Editors

Murat Yayla

Advisory Board

Arif Akşit
Figen Aksoy
Tayfun Alper
Sadet Arsan
Hediye Arslan
Oluş Api
Sebahat Atar Gürel
Tahsin Ayanoğlu
Ahmet Baschat
Nazif Bağrıaçık
Gökhan Bayhan
Yeşim Baytur
Tugan Beşe
Nur Danişmend
Fuat Demirkıran
Özgür Deren
Gönül Dinç
Melahat Dönmez

Yakup Erata
Ali Ergün
Kubilay Ertan
Bilgin Gürateş
Metin Gülmezoğlu
Arif Güngören
Melih Güven
Ayşe Kafkaslı
Ömer Kandemir
Hakan Kanit
Ömer Kılavuz
Selahattin Kumru
Asım Kurjak
Nilgün Kültürsay
Rıza Madazlı
Ercüment Müngen
Lütfü Önderoğlu
Abdurrahman Önen

Soner Öner
Semih Özeren
Okan Özkaya
Yıldız Perk
Haluk Sayman
Yunus Söylet
Mekin Sezik
Turgay Şener
Mete Tanır
Alper Tanrıverdi
Ebru Tarım
Aydın Tekay
Neslihan Tekin
Beyhan Tüysüz
Seyfettin Uludağ
Ahmet Yalınkaya

Published three times a year • Publication local periodical

Correspondence: Rumeli Caddesi 47/606, Nişantaşı 34371 İstanbul

Phone: (0212) 224 68 49 • **Fax:** (0212) 296 01 50

e-mail: editor@perinataldergi.com

www.perinataljournal.com

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All submissions to Perinatal Journal must be original, unpublished, and not under the review of any other publication.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".

Perinatal Journal follows the ethics flowcharts developed by the Committee on Publication Ethics (COPE) for dealing with cases of possible scientific misconduct and breach of publication ethics. For detailed information please visit www.publicationethics.org.

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, Technic, 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:

— **Standard journal article:** Hammerman C, Bin-Nun A, Kaplan M. Managing the patent ductus arteriosus in the premature neonate: a new look at what we thought we knew. *Semin Perinatol* 2012;36:130-8.

— **Article published in an only electronic journal:** Lee J, Romero R, Xu Y, Kim JS, Topping V, Yoo W, et al. A signature of maternal anti-fetal rejection in spontaneous preterm birth: chronic chorioamnionitis, anti-human leukocyte antigen antibodies, and C4d. *PLoS ONE* 2011;6:e16806. doi:10.1371/journal.pone.0011846.

— **Book:** Jones KL. *Practical perinatology*. New York: Springer; 1990. p. 112-9.

— **Chapter in a book:** Sibai BM, Frangieh AY. Eclampsia. In: Gleicher N, editors. *Principles and practice of medical therapy in pregnancy*. 3rd ed. New York: Appleton&Lange; 1998. p. 1022-7.

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 "jpeg" 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.

Submission

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.

Submission Checklist

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 annual 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 (undersigned by all authors)
11. Conflicts of Interest Disclosure Statement (if necessary)

Perinatal Journal

Volume 18 / Issue 3 / December 2010

Contents

Letter to the Editor	Toxoplasma Scanning During Pregnancy Ercüment Müngen	69
Research Articles	Nomogram of Fetal Cisterna Magna Width at 15-24th Gestational Weeks Resul Arısoy, Murat Yayla	72
	The Ratio of Biparietal Diameter to Nasal Bone Length Resul Arısoy, Nida Ergin, Murat Yayla, Gökhan Göynüner	79
	Turkey Demographic and Health Survey Results of Antenatal Care, Perinatal Fetal and Neonatal Evaluation With Respect to Prognosis Derya Sivri Aydın, Murat Yayla	85
	Seroprevalence of Toxoplasmosis Among Pregnant Women in Kayseri Tuba Kayman, Mesut Kayman	92
	The Impact of Placental Location on Early Fetal Growth Rahime Nida Ergin, Murat Yayla	97
Case Reports	Fetal Goiter in the Absence of Maternal Thyroid Disease: A Case Report Arif Güngören, Kenan Dolapçioğlu, Ali Ulvi Hakverdi, Ali Balcı, İsmail Güzelmansur	101
	Successful Maternal and Fetal Outcome in a Pregnancy With Type V Takayasu's Arteritis Hüseyin Levent Keskin, Olcay Turgut, Işık Üstüner, Sinan Tan, Ayşe Filiz Avşar	105
	Isolated Fetal Endocardial Fibroelastosis Diagnosed and Terminated at 22 Weeks of Gestation: A Case Report İnci Kahyaoğlu, Serkan Kahyaoğlu, Hatice Sut, Şahin Önen, Leyla Mollamahmutoğlu	109
Index	Subject and Author Index	113

LETTER TO EDITOR

Toxoplasma Scanning During Pregnancy

Ercüment Müngen

GATA, Kadın Hastalıkları ve Doğum Anabilim Dalı, İstanbul, TR

Although there are national policies about performing toxoplasma scanning on pregnant or newborns in many countries throughout the world, there is no certain policy of Turkish Ministry of Health. Different centers or physicians get their own way and consequently, management of seropositive cases drift into a complete chaos due to different views and implementations.

There are three types of protective approaches in order to prevent congenital toxoplasma infection. The purpose of primary protection is to prevent maternal infection and to inform and train mother at early pregnancy.¹ Secondary protection aims to decrease infection transition from mother to fetus and to prevent morbidity associated with toxoplasma. Tertiary protection focuses on decreasing the severity of morbidity associated with congenital toxoplasma by postnatal early diagnosis and treatment.¹ Scanning pregnant in terms of toxoplasma seropositivity is included into secondary protection and is implemented as a state policy in countries such as Austria, France, and Brasilia etc. Toxoplasma seropositivity in France is 50% while it is 80-90% in Brasilia. Spiramycine treatment and amniocentesis is applied in cases which have seroconversion during pregnancy and accepted as an acute infection.¹ If fetal infection exist as a result of PCR examination performed on amniocentesis

material, pyrimethamine and sulphonamide is administrated as preferred treatment. Termination of pregnancy is generally considered as an option only if fetal anomaly is detected in ultrasonography and family is informed for alternatives. However, there is no certain proofs that infection transition from mother to fetus and perinatal results are recovered by treating pregnant with seroconversion detected during pregnancy.^{2,3} Also, there are some problems with kits used in serological scanning of toxoplasma. Most of current Ig M kits have a serious specificity problem and cause high false positivity rates (reaching 6%).⁴ In a study researching six different Ig M kits, sensitivity rates were found between 93% and 100% while specificity rates were between 77.5% and 99.1%.⁵ Although beginning to use PCR method makes fetal diagnosis easy, the sensitivity of this method still stays below 83%.¹ While the specificity of PCR is 100% at reference laboratories, lower rates are reported in many other laboratories.¹ Another important issue is the requirement to do amniocentesis to cases with seroconversion detected by toxoplasma scanning during pregnancy. There is 0.5% (1 in 200 processes) risk of pregnancy loss in amniocentesis according to current literature. Ig M positivity is detected in 1-5% of patients in toxoplasma scanning. While some of them show acute infection, most of them are false positivity.

However, acute infection can not be eliminated by methods such as increases in Ig A titer, Ig G avidity, toxoplasma Ig G titer in some of false positive cases and therefore amniocentesis is tried. However, congenital toxoplasma prevalence is very low and it is reported as 0.73 in Sweden, 0.8 in Massachusetts, less than 1 in England, 2.4 in Finland, and 10 in France in terms of 10,000 live birth.^{1,6} Thus, fetus number to be lost in order to detect 1 congenital toxoplasma case will be unacceptably high.^{1,7} It is well known that false positive results in toxoplasma scanning, possible negative effects of medical treatment on cases detected fetal infection and uncertainties about prognosis cause serious anxiety on mother and father.⁸

Due to these scientific facts, toxoplasma scanning is not performed during pregnancy today in the USA. Serological examination is performed only in cases detected anomaly via ultrasonography. Scanning performed previously in Switzerland has been terminated recently.⁹ ACOG (American College of Obstetricians, Gynecologists) does not recommend routine toxoplasma scanning during pregnancy.¹⁰ RCOG (Royal College of Obstetricians and Gynecologists) states that it is useful to train pregnant about toxoplasma; however RCOG does not recommend routine toxoplasma scanning.¹¹ CDC (Centers for Disease Control and Prevention) emphasizes the importance of primary protection and recommends to train pregnant and women in reproductive age group about the protection against toxoplasma infection; however CDC does not recommend serological toxoplasma scanning during pregnancy.⁴ CDC also states that it would be appropriate to warn pregnant about two issues related with toxoplasma serological tests: First, no serological test can show the exact time of toxoplasma infection, and secondly, the most positive Ig M results in societies with low toxoplasma prevalence represent false positivity.⁴ In our country, toxoplasma serology does not exist among routine tests recom-

mended by Turkish Perinatology Society during pregnancy.

In this issue of Perinatology Journal, there is a study researching toxoplasma seroprevalence of pregnant in Kayseri. This study is important in terms of showing the recent status of toxoplasma prevalence in pregnant in Turkey and it contributes daily obstetric practice by emphasizing the importance of training pregnant about toxoplasma protection. On the other hand, 33.9% seropositivity found in this study is not a high rate in terms of epidemiology. This rate is low according to other studies performed in Turkey. It seems by the studies performed in other European countries that there is a similar decrease in last 2 decades. Therefore, it is not possible to agree the recommendation of authors for doing toxoplasma scanning during pregnancy in terms of the prevalence found not high and other current scientific facts mentioned above.

Consequently, it is important to train pregnant and women planning pregnancy about obeying general hygiene rules and not contacting with cats and cat droppings, eating meat products by cooking well instead of consuming them raw, not touching soil with bare hands and feet and consuming fruits and vegetables by peeling them or cleaning well in order to get protection against congenital toxoplasmosis. Serologic toxoplasma scanning is not recommended in pregnant who are not in the risk group.

References

1. Swiss Working Group on congenital Toxoplasmosis. Toxoplasmosis during pregnancy and infancy. *Swiss Med Wkly* 2008; 138(Suppl): 168.
2. Peyron F, Wallon M, Liou C, Garner P.. Cochrane Database Syst Rev. *Cochrane Database Syst Rev* 2000; (2): CD001684.
3. Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. *BMJ* 1999; 318: 1511-4.
4. CDC Preventing congenital toxoplasmosis. recommendations and reports. *MMWR* 2000; 49(RR02); 57-75.

5. Wilson M, Remington JS, Clavet C, et al. Evaluation of six commercial kits for detection of human immunoglobulin M antibodies to *Toxoplasma gondii*. *J Clin Microbiol* 1997; 35: 311-25.
6. Gilbert RE. Epidemiology of infection in pregnant women. In: Petersen E, Amboise-Thomas P, eds. Congenital toxoplasmosis: scientific background, clinical management and control. 1st ed. Paris: Springer-Verlag; 2000.
7. Bader TJ, Macones GA, Asch DA. Prenatal screening for toxoplasmosis. *Obstet Gynecol* 1997; 90: 457-64.
8. Khoshnood B, De Vigan C, Goffinet F, Leroy V. Prenatal screening and diagnosis of congenital toxoplasmosis: a review of safety issues and psychological consequences for women who undergo screening. *Prenat Diagn* 2007; 27: 395-403.
9. Stricker R, Sitavanc R, Liassine N, de Marval F. Toxoplasmosis during pregnancy and infancy. *Swiss Med Wkly* 2009; 139: 643-4.
10. American College of Obstetricians and Gynecologists. Perinatal viral and parasitic infections. Washington - ACOG Practice Bulletin 20. Washington DC: ACOG; 2000.
11. <http://www.rcog.org.uk/womens-health/clinical-guidance/infection-and-pregnancy-study-group-statement>

Nomogram of Fetal Cisterna Magna Width at 15-24th Gestational Weeks

Resul Arisoy¹, Murat Yayla²

¹S.B. Okmeydanı Eğitim ve Araştırma Hastanesi, 1. Kadın Doğum ve Hastalıkları Kliniği, İstanbul, TR

²International Hospital, Kadın Doğum ve Hastalıkları Kliniği, İstanbul, TR

Abstract

Objective: To obtain nomogram of fetal cisterna magna width at 15-24 weeks of gestation with known prognosis of normal pregnancies.

Methods: Cisterna magna width and other routine biometric measurements of 1822 structurally normal fetuses at 15-24 weeks of gestation were measured by transabdominal ultrasonography, prospectively. The distribution of cisterna magna width is established according to gestational weeks and percentiles between 15-24 weeks are calculated. Relationship between cisterna magna width and the other parameters were assessed by regression analysis.

Results: Mean values of cisterna magna width between 15-24 weeks were $3,41 \pm 0,82$ - $6,58 \pm 1,24$ mm respectively. Cisterna magna width is linearly increased between 15-24 weeks. Significant correlation was also found between the cisterna magna width (SMW) and gestational weeks (GH) ($SMW=GH \times 0.337-1.6203$ ($r^2=0.32$; $p<0.001$)), head circumference (HC) ($SMW=HC \times 0.0285+0.2137$ ($r^2=0.352$; $p<0.001$)) and biparietal diameter (BPD) ($SMW=BPD \times 0.1043+0.2681$ ($r^2=0.336$; $p<0.001$)).

Conclusion: Cisterna magna width showed a linear increase between 15-24 weeks of gestation. Gestational weeks should be taken into consideration during the evaluation of the cisterna magna width and when a value above or below the cut-off is determined, fetal ultrasonographic evaluation must be done systematically.

Keywords: Nomogram of fetal cisterna magna width at 15-24th gestational weeks.

Gebeliğin 15-24 haftalarında sisterna magna genişliğinin nomogramı

Amaç: Prognozu bilinen normal gebeliklerde 15-24. gebelik haftalarında fetüsün sisterna magna genişliğinin nomogramının elde edilmesi.

Yöntem: Bu prospektif çalışmada 15-24. gebelik haftalarında yapısal olarak normal 1822 fetusa ait fetal biyometrik ölçümler transabdominal ultrasonografi ile yapıldı. Bu fetüslerin sisterna magna genişliğinin gebelik haftalarına göre dağılımı çıkarıldı ve 15-24. gebelik haftaları arasında persantil değerleri hesaplandı. Sisterna magna genişliği ile diğer biyometrik parametreler arasında regresyon analizi yapıldı.

Bulgular: 15-24 gebelik haftaları arasında ortalama sisterna magna genişliği (SMG) sırasıyla $3,41 \pm 0,82$ - $6,58 \pm 1,24$ mm arasında tespit edildi. Sisterna magna genişliğinin gebelik haftası (GH) ile ilişkisi incelendiğinde, 15-24 gebelik haftaları arasında lineer olarak arttığı saptandı. Lineer regresyon analizinde; ($SMG=GH \times 0.337-1.6203$ ($r^2=0.32$; $p<0,001$)), baş çevresi (HC) ($SMG=HC \times 0.0285+0.2137$ ($r^2=0.352$; $p<0.001$)) ve bipariyetal çap (BPD) ($SMG=BPD \times 0.1043+0.2681$ ($r^2=0,336$; $p<0.001$)) arasında anlamlı korelasyon saptandı.

Sonuç: Sisterna magna genişliği 15-24 gebelik haftaları arasında lineer bir artış göstermiştir. Sisterna magna genişliğinin değerlendirilmesinde gebelik haftası göz önünde bulundurulmalı ve uç değerlerin saptanması durumunda fetusta sistematik fetal ultrasonografik inceleme yapılmalıdır.

Anahtar Sözcükler: Sisterna magna genişliği, baş çevresi, gebelik haftası nomogram.

Introduction

Central nervous system develops from the structure called neural plate which is formed with thickening of ectoderm layer after fifth gestational week. Cisterna magna (cisterna cerebellomedullaris) is one of the enlargements made by subarachnoid interval (in which cerebrospinal fluid circulates) on brain base and it is limited with occipital bone, medulla oblongata and cerebellum.^{1,5} While cerebral structures are observed in fetal examinations, it is one of the sonoluscent cavities that should be paid attention and it is observed on third axial plan. Sagittal and coronal plans also should also be examined in their pathologies.² It may be confused terminologically with posterior fossa which is between foramen magnum and tentorium cerebelli and includes mid-cerebrum, pons, cerebellum, medulla oblongata and interior surface of occipital bone.⁴

The width of cisterna magna (SMG) is the measurement of the distance between posterior edge of cerebellar vermis and interior surface of occipital bone. Normal width is 2-10 mm.⁵ However, cerebellar vermis is not fully developed at second trimester and observing at early weeks may cause to misevaluate normal appearance. Therefore, exact evaluation of cisterna magna and posterior fossa should not be performed before 18th gestational week.^{2,6}

Pilu et al. researched posterior fossa structures of 19 fetuses with spina bifida in their prospective study and reported that the diameter of transverse cerebellar was shorter than normal in all cases and cisterna magna was obliterated.⁷ The obliteration (<2 mm) or non-appearance of cisterna magna was associated with neural tube defects and Arnold Chiari Type 2 malformation in many studies.⁸⁻¹⁴ While mega cisterna magna (>10 mm) can be with structural (Dandy Walker Malformation, arachnoid cyst) or chromosomal anomalies, it also can exist in normal fetuses in an isolated way.¹⁵⁻¹⁹

In this study, we aimed to obtain the nomogram of SMG in normal pregnancies in our population and to evaluate its relationship with GW (gestational week), BPD (biparietal diameter) and head circumference (HC).

Methods

1822 pregnant women chosen prospectively in between 01.01.2006 and 01.01.2010 were included into our study. Our study was formed of single pregnancies between 15th and 24th gestational weeks. Last menstruation date for pregnancy week, head-back distance at first trimester for those with unknown menstruation date or biparietal diameter measurements at second trimester were based on. Those with structural defect or karyotype anomaly, multiple pregnancies, those who gave stillbirth, those with early membrane rupture and intrauterine growth retardation and with systemic disease were excluded from the study.

Ultrasonographic measurements were performed via Voluson 730 (General Electric, USA) ultrasonography device with a transabdominal approach (2-8 MHz) by a single operator. The measurement of SMG was performed by taking the furthest distance between posterior edge of cerebellar vermis and interior surface of occipital surface on suboccipitobregmatic plan where thalamus, cavum septum pellucidum, cerebellum, cisterna magna and nuchal translucency are seen together. Normal SMG is shown in Figure 1 and expanded SMG is shown in Figure 2. Other biometric measurements (BPD, HC) related with the fetus head were completed.

SPSS 11.0 software was used in statistical analyses. SMG was taken as dependent variable in descriptive statistical analyses and linear regression analyses were performed by matching with GW, BPD and HC. The relationship of dependent and independent variables were evaluated by Pearson correlation test. One-way Anova, Post Hoc-Test (Tukey HSD method) analyses were done. Percentile values of SMG



Figure 1. Normal cisterna magna width.



Figure 2. Abnormal cisterna magna width.

according to weeks in between 15th and 24th gestational weeks were calculated. Results were evaluated at $p < 0.05$ significance level within 95% confidence interval.

Results

In our study, age range of pregnant complying with research criteria was 19-45 and their mean age was 30.97 ± 4.32 . Examined gestational week range was 15-24 and their mean gestational week was 20.96 ± 2.14 .

Mean SMG between 15th and 24th gestational week was 3.41 ± 0.82 - 6.58 ± 1.24 , respectively. SMG was found significantly different according to gestational weeks and there is pos-

itive correlation with gestational week. SMG measurements according to gestational week at 95% confidence interval are given in Table 1 and the distribution of SMG percentiles according to gestational week is given in Table 2.

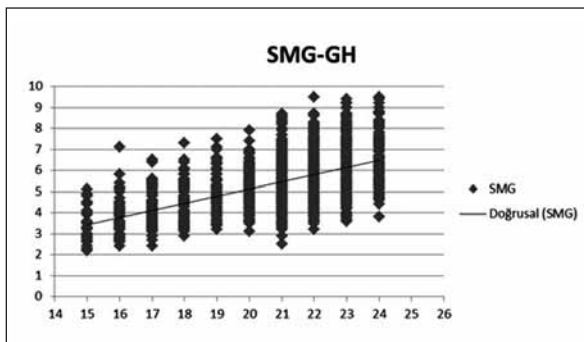
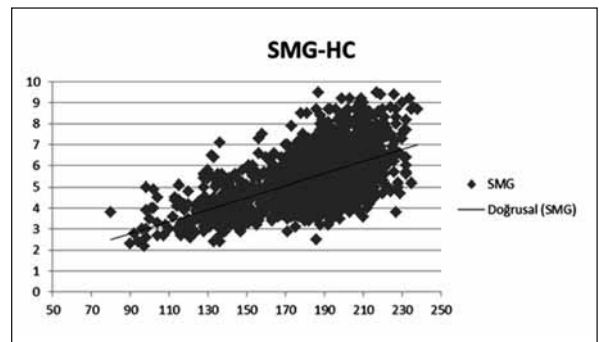
Regression equation by linear regression analysis between SMG and GW is given as $SMG = GW \times 0.337 - 1.6203$ ($r^2=0.32$; $p < 0.001$) (Diagram 1). Regression equation by linear regression analysis between SMG and BPD is given as $SMG = BPD \times 0.1043 + 0.2681$ ($r^2=0.336$; $p < 0.001$) Regression equation by linear regression analysis between SMG and HC is given as $SMG = HC \times 0.0285 + 0.2137$ ($r^2=0.352$; $p < 0.001$) (Diagram 2). It is seen that SMG exhibits correlation mostly with HC.

Table 1. Measurement results of cisterna magna width according to gestational week at 95% confidence interval.

GW	N	Average	Std. Dev.	Std. Error	Minimum	Maximum
15	28	3.41	0.82	0.15	2.2	5.1
16	63	3.78	0.83	0.10	2.4	7.1
17	117	4.06	0.74	0.07	2.4	6.5
18	76	4.49	0.92	0.11	2.9	7.3
19	78	4.92	0.92	0.11	3.2	7.5
20	174	5.10	0.91	0.07	3.1	7.9
21	388	5.44	1.05	0.05	2.5	8.7
22	468	5.81	1.11	0.05	3.2	9.5
23	321	6.07	1.19	0.07	3.6	9.4
24	109	6.58	1.24	0.12	3.8	9.5
Total	1822	5.44	1.28	0.03	2.2	9.5

Table 2. Percentile distribution of cisterna magna width according to pregnancy week.

Gestational week	Percentiles						
	5	10	25	50	75	90	95
15	2.25	2.39	2.80	3.25	4.00	4.81	5.01
16	2.70	2.74	3.30	3.60	4.10	4.88	5.36
17	3.08	3.20	3.60	3.90	4.40	5.30	5.50
18	3.20	3.40	3.73	4.40	5.10	5.80	6.15
19	3.40	3.79	4.38	4.80	5.50	6.31	6.62
20	3.68	3.90	4.50	5.00	5.73	6.30	6.80
21	4.00	4.20	4.70	5.40	6.18	6.90	7.20
22	4.10	4.40	5.00	5.70	6.60	7.30	7.66
23	4.30	4.60	5.20	6.00	6.80	7.78	8.20
24	4.70	5.00	5.60	6.40	7.45	8.40	8.80

**Diagram 1.** The distribution of cisterna magna width according to gestational week.**Diagram 2.** The distribution of cisterna magna width according to head circumference.

Discussion

It was shown in many studies that the width of cisterna magna increased with gestational week and its normal range was 2-10 mm.^{5,11,19-21} Mahony et al. reported SMG in their study as averagely 5 ± 3 mm on 219 pregnant at or after 15th gestational week. They called mega or wide cisterna magna when the width is above 10 mm. Also they reported that isolated wide cisterna magnas are clinically not significant.⁵ In our study, we found that SMG increased linearly with gestational week ($r^2=0.32$, $P<0.001$) and showed significant difference according to gestational week. We found mean SMG as 5.44 ± 1.28 mm.

Haimovici et al. researched prognosis of 15 fetuses of whom isolated wide cisterna magna (11-19 mm) was examined in between 26th and

37th gestational weeks. All of these pregnancies were resulted with normal phenotype newborns and all eight cases which were reached in their long-term (2-69 months) follow-ups were reported as normal.²² Dror et al. compared 29 fetuses having wide cisterna magna with 35 normal fetuses in terms of their development. When children were evaluated by Gesell Development Schedules and Peabody Developmental Motor Scale, it was reported that study group had a significantly worse performance at Gesell test; however, general performance of both groups was within normal limits. It was reported that walking age was statistically and significantly late in the study group. Consequently, it was emphasized in this study that children with wide cisterna magna

are under risk in terms of slight growth retardation.²³

Steiger et al. reported that SMG had a better correlation ($r^2=0.54$ $P<0.001$) during 15th–35th gestational weeks.¹⁸ In our study, we thought that the reason for being weaker of this correlation was gestational weeks we examined which were more limited than those of Steiger et al. Thus, mean cisterna magna widths we found during 15th–24th gestational weeks are similar with the results of the study performed by Steiger et al. (Table 3).

We found in our study that SMG increased with BPD ($r^2=0.336$) and HC ($r^2=0.352$) linear-

ly. It was reported in the study of Köktener et al. performed on 194 fetuses between 16th–24th gestational weeks that SMG was in correlation mostly with GW ($r^2=0.75$ $P<0.001$) and also there was a linear correlation with BPD ($r^2=0.74$ $P<0.001$).²⁰ However, this correlation coefficients were very high because of the low number of cases. Also in our study, the correlation of SMG with HC and BPD was found higher than the correlation with gestational week.

No difference was found between the percentile distribution of SMG given in the study of Snijders and Nicolaides²¹ with the percentile distribution given in our study (Table 4).

Table 3. The comparison of current study values with the study of Steiger et al.¹⁷

GW	Current study		The study of Steiger et al.	
	Average	Std. deviation	Average	Std. deviation
15	3.4	0.8	3.3	0.9
16	3.8	0.8	3.7	0.9
17	4.1	0.7	3.8	0.9
18	4.5	0.9	4.6	1.1
19	4.9	0.9	5.1	1.2
20	5.1	0.9	5.5	1.0
21	5.4	1.1	5.5	1.3
22	5.8	1.1	6.2	1.5
23	6.1	1.2	6.4	1.5
24	6.6	1.2	6.2	1.5

Table 4. The comparison of percentile values of current study with the study of Snijders et al.²⁰

GH	Percentile values of current study			Percentile values of Snijders and Nicolaides		
	5	50	95	5	50	95
15	2.3	3.3	5.0	2.1	3.5	5.3
16	2.7	3.6	5.4	2.4	3.8	5.7
17	3.1	3.9	5.5	2.6	4.1	6
18	3.2	4.4	6.2	2.8	4.3	6.3
19	3.4	4.8	6.6	3.1	4.6	6.6
20	3.7	5.0	6.8	3.3	4.9	7.2
21	4.0	5.4	7.2	3.5	5.1	7.5
22	4.1	5.7	7.7	3.7	5.4	7.7
23	4.3	6.0	8.2	3.9	5.6	8
24	4.7	6.4	8.8	4.1	5.8	8.2

Nicolaides et al. included 70 fetuses into their retrospective study which were established the diagnosis of open spina bifida by ultrasonography during 16th–23rd gestational weeks and they reported that cerebellar hemisphere bent forward in 12 (57%) of 21 fetuses with suboccipitobregmatic view in cranium and they had also cisterna magna obliteration (banana sign) synchronously.⁸ Campbell et al. scanned 436 fetuses who were at high risk in terms of fetal anomaly and 26 of them were established open spina bifida diagnosis, and 16 fetuses (62%) were reported as having banana sign (Chiari II malformation).⁹ Goldstein et al. reported in their study that cisterna magna was gone in 18 of 19 case with meningomyelocele of whom posterior fossa could be followed well and one case had very narrowed cisterna magna. Also they were reported that cisterna magna was gone in 5 of 13 cases with isolated Ventriculomegaly of whom posterior fossa could be followed well.¹¹

Ghi et al. followed up 57 of 66 fetuses that they diagnoses as spina bifida during 16th–34th gestational weeks and defined 93% of these cases as open defect and 7% of them as closed defect. During mid-gestation, they always found open defect cases with banana sign and lemon sign. However, they detected ventriculomegaly only in 64.2% of cases with open defect. They reported that intracranial anatomy was normal in those with closed defect diagnosed lately.¹³ Güven et al. found in their study that there was enlarged cisterna magna in 60% of cases (3/5) with Dandy-Walker malformation and in 13% of cases (1/3) with Dandy-Walker variant.¹⁵ It was reported in the study of Filly et al. that brain and spinal cord anomaly risk was 0.005% in fetuses who had normal cisterna magna and lateral ventricle.¹⁰

Nyberg et al. evaluated 33 fetuses with wide cisterna magna in their study in terms of chromosomal anomaly and found normal karyotype in 15 fetuses and chromosomal anomaly

in 18 fetuses. 12 of chromosomal anomalies were reported as Trisomia 18, 3 of them as Trisomia 13, one of them as 45 X0, one of them as 46 XX t(21q) and one of them as 46,XY del(6 q25). Also it was reported that there was an advanced correlation between wide chromosomal anomalies and wide cisterna magnas which were not accompanied by Ventriculomegaly.¹⁷

Steiger et al. stated in their study that the sensitivity of +2.5 SD value of SMG was low for Trisomia 18.¹⁸ It was reported in the study performed by Watson et al. that SMG measurement during 14th–21st gestational weeks was not helpful for scanning chromosomal anomalies.¹⁹

Conclusion

Consequently, cisterna magna width exhibits a linear increase in between 15th and 24th gestational weeks. This increase is closely associated with BPD and especially HC. Evaluating the width of cisterna magna may enable to establish early diagnosis of defects and anomalies which may exist in posterior fossa and adjacent organs. Gestational week should be considered while performing this evaluation and systematic ultrasonographic examination should be done on fetus if extreme values are detected.

References

1. Kostavic-Knezevic L, Gojovic S, Mitrecic D. Development of the Human Embryo. In: Kurjak A, Chervenak FA (Ed). *Ultrasound Obstetrics Gynecology* 2nd edition. New Delhi: Jaypee; 2008; pp. 143-51.
2. Filly RA, Feldstein VA. *Ultrasound Evaluation of Normal Fetal Anatomy*. In: Callen PW (Ed). *Ultrasonography In Obstetrics And Gynecology*. 5th ed. Amsterdam: Elsevier; 2007; pp. 297-362.
3. Kollias SS, Ball WS Jr, Prenger EC. Cystic malformations of the posterior fossa: Differential diagnosis clarified through embryologic analysis. *Radiographics* 1993; 13: 1211-31.
4. Nishikawa M, Sakamoto H, Hakuba A, Nakanishi N, Inoue Y. Pathogenesis of Chiari malformation: a morphometric study of the posterior cranial fossa. *J Neurosurg* 1997; 86: 40-7.

5. Mahony BS, Callen PW, Filly RA, Hoddick RA. The fetal cisterna magna. *Radiology* 1984; 153: 773-6.
6. Bromley B, Nadel AS, Pauker S, Estroff JA, Benacerraf BR. Closure of the cerebellar vermis: evaluation with second trimester US. *Radiology* 1994; 193: 761-3 .
7. Pilu G, Romero R, Reece EA, Goldstein I, Hobbins JC, Bovicelli L. Subnormal cerebellum in fetuses with spina bifida. *Am J Obstet Gynecol* 1988; 158: 1052-6.
8. Nicolaides KH, Campbell S, Gabbe SG, Guidetti R. Ultrasound screening for spina bifida: cranial and cerebellar signs. *Lancet* 1986; 12: 72-4.
9. Campbell J, Gilbert WM, Nicolaides KH, Campbell S. Ultrasound screening for spina bifida: cranial and cerebellar signs in a high-risk population. *Obstet Gynecol* 1987; 70: 247-50.
10. Filly RA, Cardoza JD, Goldstein RB, Barkovich AJ. Detection of fetal central nervous system anomalies: a practical level of effort for a routine sonogram. *Radiology* 1989; 172: 403-8.
11. Goldstein RB, Podrasky AE, Filly RA, Callen PW. Effacement of the fetal cisterna magna in association with myelomeningocele. *Radiology* 1989; 172: 409-13.
12. Van den Hof MC, Nicolaides KH, Campbell J, Campbell S. Evaluation of the lemon and banana signs in one hundred thirty fetuses with open spina bifida. *Am J Obstet Gynecol* 1990; 162: 322-7.
13. Ghi T, Pilu G, Falco P, Segata M, Carletti A, Cocchi G, Santini D, Bonasoni P, Tani G and Rizzo N. Prenatal diagnosis of open and closed spina bifida. *Ultrasound Obstet Gynecol* 2006; 28: 899-903.
14. Tosun A, Bozan BS. Chiari tip II olgusunda obstetrik ultrasonografi bulguları. *Dicle Tıp Dergisi* 2009; 36: 310-3.
15. Güven MA, Ceylaner S, Ceylaner G. Dandy walker malformation and variation: Prenatal ultrasonographic features and clinical outcome. *Perinatal Journal* 2004; 12: 173 -8.
16. Novakov-Mikić A, Koprivsek K, Lucić M, Belopavlović Z, Stojić S, Sekulić S. Prenatal diagnosis of posterior fossa anomalies—an overview. *Med Pregl* 2009; 62: 157-63.
17. Nyberg DA, Mahony BS, Hegge FN, Hickok D, Luthy DA, Kapur DR. Enlarged cisterna magna and the Dandy-Walker malformation: Factors associated with chromosome abnormalities. *Obstet Gynecol* 1991; 77: 436-42.
18. Steiger RM, Porto M, Lagrew DC, Randall R. Biometry of the fetal cisterna magna: estimates of the ability to detect trisomy 18. *Ultrasound Obstet Gynecol* 1995; 5: 384-90.
19. Watson WJ, Katz VL, Chescheir NC, Miller RC, Menard MK, Hansen WF. The cisterna magna in second-trimester fetuses with abnormal karyotypes. *Obstet Gynecol* 1992; 79: 723-5.
20. Kokter A, Dilmen G, Kurt A. The cisterna magna size in normal second-trimester fetuses. *J Perinat Med* 2007; 35: 217-9.
21. Snijders BJM, Nicolaides KH. Fetal biometry at 14-40 weeks' gestation. *Ultrasound Obstet Gynecol* 1994; 4: 34-48.
22. Haimovici JA, Doubilet PM, Benson CB, Frates MC. Clinical significance of isolated enlargement of the cisterna magna (>10mm) on prenatal sonography. *J Ultrasound Med* 1997; 16: 731-4.
23. Dror R, Malinger G, Ben-Sira L, Lev D, Pick CG, Lerman-Sagie T. Developmental outcome of children with enlargement of the cisterna magna identified in utero. *J Child Neurol* 2009; 24: 1486-92.

The Ratio of Biparietal Diameter to Nasal Bone Length

Resul Arısoy¹, Nida Ergin², Murat Yayla², Gökhan Göynüner³

¹Sağlık Bakanlığı Okmeydanı Eğitim Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, TR

²International Hospital, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, TR

³Sağlık Bakanlığı Göztepe Eğitim Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, TR

Abstract

Objective: The aim of this study was to determine the relationship between the ratio of biparietal diameter to nasal bone length and gestational weeks at the second trimester of pregnancy.

Methods: We evaluated consecutively fetuses referred to our facility between 15 and 22 weeks' gestation for perinatal sonography and amniocentesis because of an increased risk of aneuploidy. Anatomically normal and euploid 505 fetuses were included in the study. A detailed structural survey, biometric measurements, and measurement of the nasal bone were obtained before the amniocentesis procedure. The distribution of fetal nasal bone length between 15-22 gestational weeks was established and their percentiles were calculated. The ratio of biparietal diameter to nasal bone length was calculated for each case.

Results: The mean nasal bone length for 15 to 22 week's gestation was 3.21±0.41, 3.45±0.52, 3.81±0.58, 4.17±0.68, 4.42±0.66, 4.89±0.89, 5.35±0.90 and 5.84±1.02 mm respectively. A significant positive correlation was also found between the nasal bone length and the gestational week (Nasal bone length = -2.485+0.370xGestational week (r²=0.50; p<0.001)). The mean biparietal diameter/nasal bone length ratio was 9.94±1.56 and did not progressively increase with advancing gestational age.

Conclusion: The ratio of biparietal diameter to nasal bone length remained constant at 15-22 gestational weeks.

Keywords: Nasal bone length, gestational week, the ratio of biparietal diameter to nasal bone length.

Bipariyetal çapın burun kemiği uzunluğuna oranı

Amaç: Çalışmamızda gebeliğin ikinci trimesterinde bipariyetal çapın burun kemiği uzunluğuna oranının gebelik haftası ile ilişkisini değerlendirmeyi amaçladık.

Yöntem: Gebeliğin 15-22 haftaları arasında perinatal ultrasonografi ve amniosentez için sevk edilen normal karyotipli ve anomalisi olmayan 505 fetus çalışmaya dahil edildi. Fetal biyometri ve burun kemiği ölçümleri amniosentez işlemi öncesinde elde edildi. Ölçümlerle birlikte fetal yapılar ayrıntılı olarak değerlendirildi. Burun kemiği uzunluğunun 15-22 gebelik haftaları arasında dağılımı ve yüzdelik değerleri çıkarıldı. Her fetus için bipariyetal çapın burun kemiği uzunluğuna oranı bulunarak gebelik haftası ile olan ilişkisi değerlendirildi.

Bulgular: Gebeliğin 15-22 haftaları arasında ortalama burun kemiği uzunluğu sırasıyla 3.21±0.41, 3.45±0.52, 3.81±0.58, 4.17±0.68, 4.42±0.66, 4.89±0.89, 5.35±0.90 ve 5.84±1.02 mm olarak saptandı. Burun kemiği uzunluğunun gebelik haftası ile birlikte lineer olarak arttığı ve bu korelasyonun anlamlı olduğu bulundu. Burun kemiği uzunluğu ile gebelik haftası arasındaki lineer regresyon analizi ile regresyon denklemi şu şekilde oluşturuldu: Burun kemiği uzunluğu = -2.485+0.370xGebelik haftası (r²=0.50; p<0.001). Fakat gebelik haftaları ile bipariyetal çapın burun kemiği uzunluğuna oranının anlamlı olarak değişmediği (p>0.05) ve bipariyetal çapın burun kemiği uzunluğuna oranının ortalama 9.94±1.56 olduğu bulundu.

Sonuç: Bipariyetal çapın burun kemiği uzunluğuna oranı gebeliğin 15-22 haftaları arasında sabit değer göstermektedir.

Anahtar Sözcükler: Burun kemiği uzunluğu, gebelik haftası, bipariyetal çapın burun kemiği uzunluğuna oranı.

Introduction

Nasal bone begins to develop as two separate structures from neural crest cells at sixth gestational week. Both structures ossify through intramembranous ossification. It can be seen by ultrasonography after the 10th gestational week.^{1,2} The experience of physician using ultrasonography, device quality, the appropriateness of the plan examined, oligohydramnios, obesity, fetus position and gestational week may affect examination quality.³

It was shown in previous studies that detecting non-existence or hypoplasia of nasal bone is an effective method for scanning chromosomal anomalies.^{4,5} Langdon Down stated in 1866 that nasal bone shortness is a common characteristic of patients with Trisomia 21 and then this syndrome is named after him later.⁶ It was reported that 60% of fetuses with non-existence or hypoplasia of nasal bone in between 14th and 25th gestational weeks had Trisomia 21 and that the rate of hypoplasia occurrence in those with euploid was 1.4%.² Cicero et al. defined in their studies performed on 1046 pregnant between 15th and 22nd gestational week that the nasal bone hypoplasia is the nasal bone length (NBL) below 2.5 mm. Nasal bone hypoplasia rates were 61.8% in fetuses with Trisomia, 3.3% in fetuses with chromosomal anomalies and 1.2% in normal fetuses.⁷ Bunduki et al. reported in their study performed on pregnant between 16th and 24th gestational weeks that nasal bone hypoplasia is the NBL below 5th percentile and specified the sensitivity for Trisomia 21 as 59.1%.⁸

Determining non-existence or hypoplasia of nasal bone is accepted as an effective method today for scanning chromosomal anomalies. While it is required to know nasal bone lengths as to weeks in order to detect nasal hypoplasia, other non-changing rates supporting this finding are also required.⁴

In this study, nasal bone length and the change of rate of biparietal diameter to nasal bone length (BPD/NBL) according to gestation-

al week for fetuses with normal karyotype and no anomaly were researched and the relationship between them were analyzed.

Method

The study was performed on 584 pregnant who were examined by perinatal ultrasonography and than had karyotype analysis in between 01.01.2006 and 01.07.2010. Last menstruation date for pregnancy week, head-back distance at first trimester for those with unknown menstruation date or biparietal diameter measurements at second trimester were based on. Those with structural defect or karyotype anomaly, multiple pregnancies, those who gave stillbirth, those with early membrane rupture and intrauterine growth retardation and with systemic disease were excluded from the study. The study group was formed of 505 single pregnancies with normal karyotype analysis and not having congenital anomaly that were chosen prospectively in between their 15th and 22nd gestational weeks. 79 pregnancies were excluded from the study. The reason for excluding them was that structural anomaly was found in 34 of these pregnancies, chromosomal anomaly was found in 33 of them (also there was structural anomaly in 12 fetuses) and missed abortus found in one of them, and also five pregnant due to systemic diseases were excluded from the study and six pregnant due to not having follow-up.

Ultrasonographic measurements were performed via General Electric Voluson 730 (USA) ultrasonography device with a transabdominal approach (2-7 MHz) by a single operator. Biometric evaluation of the fetus was performed. Fetal biometry and nasal bone measurements were obtained before amniocentesis. BPD measurement was performed by taking the distance from posterior edge of frontal parietal bone to interior surface of posterior parietal bone on cranium axial plan where thalamus, cavum septum pellucidum and third ventricle are seen together. Nasal bone was imaged

with low brightness adjustment and 45 or 135 degree angle within the area where maxilla and frontal bone are limited in the plan where jaw and lips of fetus are displayed on midsagittal facial profile. Measurements were done as the maximum length between upmost and lowermost ends of nasal bone. The average value was obtained by performing these measurements twice. BPD/NBL rate was calculated for each fetus. Lengths and rates were compared with gestational week.

Patient data were analyzed by SPSS 11.5 software (SPSS Inc., Chicago, IL, USA). Pearson Correlation test, Regression analyzes and descriptive statistical analyses were performed. One-way variance analysis (One-way Anova) and Post Hoc comparison test were performed by Tukey’s HSD method. Results were evaluat-

ed at $p < 0.05$ significance level within 95% confidence interval.

Results

505 pregnant complying with research criteria were included into our study. Age range of these pregnant was 18-47, and the mean age was 34.41 ± 5.10 . Gestational week range was 15-22 for the study, and mean gestation week was found as 17.84 ± 1.80 . Mean NBL was 4.12 ± 0.94 mm and BPD was 39.93 ± 5.94 mm.

It was found in our study that NBL increased linearly with gestational week (GW) and this correlation was significant. The regression equation between NBL and GW was found as $NBL = -2.485 + 0.370 \times GW$ ($r^2 = 0.50$; $p < 0.001$) by linear regression analysis (Diagram 1). NBL

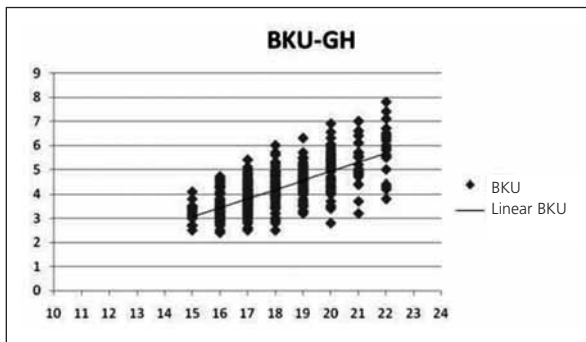


Diagram 1. Nasal bone length according to gestational week.

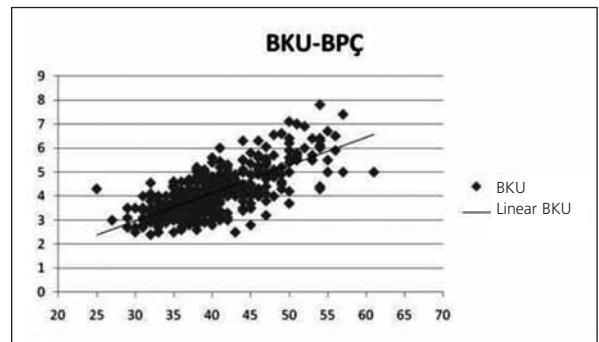


Diagram 2. Nasal bone length according to biparietal diameter.

Table 1. NBL measurements according to gestational week within 95% confidence interval.

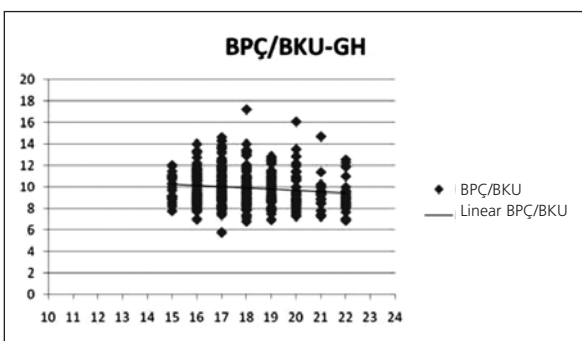
At 95% confidence interval								
GW	N	Average	Std. Dev.	Std. Error	Lower limit	Upper limit	Minimum	Maximum
15	21	3.21	0.41	0.09	3.01	3.39	2.5	4.1
16	104	3.45	0.52	0.05	3.35	3.56	2.4	4.7
17	141	3.81	0.58	0.05	3.71	3.91	2.5	5.4
18	84	4.17	0.68	0.08	4.03	4.32	2.5	6.0
19	58	4.42	0.66	0.09	4.25	4.59	3.2	6.3
20	43	4.89	0.89	0.14	4.62	5.17	2.8	6.9
21	31	5.35	0.90	0.16	5.02	5.68	3.2	7.0
22	23	5.84	1.02	0.21	5.40	6.28	3.8	7.8
Total	505	4.12	0.94	0.04	4.04	4.20	2.4	7.8

Table 2. NBL distribution according to gestational week.

GW	Percentiles		
	5	50	95
15	2.5	3.2	4.1
16	2.7	3.4	4.4
17	3.0	3.8	4.8
18	3.0	4.2	5.3
19	3.3	4.4	5.5
20	3.4	5.0	6.5
21	3.5	5.2	7.0
22	3.9	5.9	7.7

measurements according to gestational week within 95% confidence interval are given in Table 1 and percentile distributions are given in Table 2. The regression equation between NBL and BPD was found as $NBL = -0.529 + 0.116 \times BPD$ ($r^2=0.54$; $p<0.001$) by linear regression analysis (Diagram 2). It was seen that nasal bone length displayed most correlation with BPD in between 15th and 22nd gestational weeks.

It was observed in our study that nasal bone length displayed diversity significantly among groups formed according to the gestational weeks. However, BPD/NBL rate did not change significantly ($P>0.05$) and mean BPD/NBL rate was 9.94 ± 1.56 (Diagram 3). When 11, 12 and 13 were taken as the limit value of BPD/NBL for scanning, false positivity rates were found as 21.8%, 10.5% and 4.2%, respectively.

**Diagram 3.** The relationship of BPD/NBL rate with gestational week.

Discussion

In our study, it was found that nasal bone length increases linearly with gestational week ($r^2=0.50$) and it was averaged 4.12 ± 0.94 mm. Guis et al. reported in their study that mean nasal bone length was between 4 and 12 mm and it displayed an increase linear with gestational week ($r^2=0.68$).⁹ Sonek et al. measured nasal bone length in 3537 pregnancies in between 11th and 40th gestational weeks and reported that this length displayed a positive correlation with gestational week ($r^2=0.77$).¹⁰ Bunduki et al. found mean nasal bone length as 6.9 ± 1.29 mm in their study performed on 1631 fetuses between 16th and 24th gestational weeks and stated that there was a linear increase with gestational week.⁸ Yayla et al., Naraphut et al., and Sutthibenjakul et al. reported that nasal bone length increased linearly with gestational week.^{3,11,12}

The relation level between NBL and GW ($r^2=0,43$) found in the study of by Jung et al. on 3019 fetuses in between 16th and 28th gestational week was similar to our study.¹³ Nasal bone length was shorter in our study than found in other national studies. It is considered that this is caused by high risky pregnancies forming the study group, and technical, ethnical and racial differences (Table 3). In fact, Zelop et al. reported that nasal bone length may vary among ethnical origin and races.¹⁴ Also we could not compare properly the studies of Yayla et al. and Yalınkaya et al. performed on NBL in our study.^{3,15} The reason was that both study groups (polyclinic patients without karyotype anomaly risk) and studied gestational weeks (11-39 GW) and (11-41 GW) were different and mean NBL and percentile values according to gestational weeks were not analyzed in these studies.

Bromley et al. measured nasal bone length of 239 fetuses with high risk in between 15th and 20th gestational week and found that the rate of BPD/NBL did not change with gestational week and only one limit value could be used.

Table 3. 5th percentile values of current study and other studies between 15th and 22nd GW.

GW	5th Percentile NBL				
	Bundaki et al. ⁷	Sonek et al. ¹⁰	Naraphut et al. ¹¹	Sutthibenjakul et al. ¹²	Current study
15	-	3.0	2.6	2.5	2.5
16	4.1	3.4	3.0	3.0	2.7
17	4.3	4.0	3.4	3.3	3.0
18	4.6	4.3	3.7	3.6	3.0
19	4.9	5.0	4.1	4.2	3.3
20	5.2	5.2	4.5	4.8	3.4
21	5.4	5.6	4.9	5.7	3.6
22	5.7	5.8	5.3	6.1	3.9

Mean BPD/NBL rate in fetuses with normal karyotype was reported as 8.1 ± 1.4 while it was 11.3 ± 2.0 in fetuses with Trisomia 21 and the difference was significant. Also, it was reported that false positivity rates were 22%, 11.5% and %2 respectively when BPD/NBL rates were 9, 10, 11 and 12.⁴ Obido et al. found the sensitivity of scanning Down syndrome as 59% and false positivity as 15% when BPD/NBL rate was ≥ 11 .¹⁶ Tran et al. also stated that BPD/NBL rate was a significant and independent marker for Down syndrome.¹⁷ In our study, we found mean BPD/NBL rate as 9.94 ± 1.56 and that it was not changing with gestational week similar to other studies. When BPD/NBL limit value for scanning was taken 11, 12, and 13, false positivity rate was found as 21.8%, 10.5% and 4.2% and these rates were found high according to the literature.

Conclusion

Consequently, we found in our study that nasal bone length increased linearly with gestational week. However, we found that BPD/NBL rate was not changing with gestational week and this rate was 9.9 ± 1.5 . We observed that it could be pathological with 4% false positivity when BPD/NBL rate was 13 and above. We considered that fetuses might need more advanced analyses in diagnosis with this measurement and above, and the diagnoses in cases with anomaly should be compared with current

diagnoses in order to do that and secondary studies are needed to examine them, and the related rate could be used securely only by these studies.

References

1. Sonek JD, Cicero S, Neiger R and Nicolaidis KH. Nasal bone assessment in prenatal screening for trisomy 21. *Am J Obstet Gynecol* 2006; 195: 1219-30.
2. Sandikcioglu M, Molsted K and Kjaer I. The prenatal development of the human nasal and vomeral bones. *J Craniofac Genet Dev Biol* 1994; 14: 124-34.
3. Yayla M, Göynümer G, Uysal Ö. Fetal nasal bone length nomogram. *Perinatal Journal* 2006; 14:77-82.
4. Bromley B, Lieberman E, Shipp TD, Benacerraf B. Fetal nose bone length: a marker for Down syndrome in the second trimester. *J Ultrasound Med* 2002; 21: 1387-94.
5. Gianferrari EA, Benn PA, Dries L, Brault K, Egan JF, Zelop, CM. Absent or shortened nasal bone length and the detection of Down syndrome in second-trimester fetuses. *Obstet Gynecol* 2007; 109: 371-5.
6. Down LJ. Observations on an ethnic classification of idiots. Clinical Lectures and Reports. *London Hospital* 1866; 3: 259-62.
7. Cicero S, Sonek JD, McKenna DS, Croom CS, Johnson L and Nicolaidis KH. Nasal bone hypoplasia in fetuses with Trisomy 21 at 15-22 weeks' gestation. *Ultrasound Obstet Gynecol* 2003; 21: 15-8.
8. Bunduki V, Ruano R, Miguez J, Yoshizaki CT, Kahhale S, Zugaib M. Fetal nasal bone length: reference range and clinical application in ultrasound screening for trisomy 21. *Ultrasound Obstet Gynecol* 2003; 21: 156-60.
9. Guis F, Ville Y, Vincent Y, Doumerc S, Pons J, Frydman R. Ultrasound evaluation of the length of the fetal nasal bones throughout gestation. *Ultrasound Obstet Gynecol* 1995; 5: 304-7.

10. Sonek JD, Mckenna D, Webb D, Croom C, Nicolaides KH. Nasal bone length throughout gestation: normal ranges based on 3537 fetal ultrasound. *Ultrasound Obstet Gynecol* 2003; 21: 152-5.
11. Naraphut B, Uerpaiojkit B, Chaithongwatthana S, Tannirandorn Y, Tanawattanacharoen S, Manotaya S, Charoenvidhya D. Nasal bone hypoplasia in trisomy 21 at 15 to 24 weeks' gestation in a high risk Thai population. *J Med Assoc Thai* 2006; 89: 911-7.
12. Sutthibenjakul S, Suntharasaj T, Suwanrath C, Kor-anantakul O, Geater A. A Thai reference for normal fetal nasal bone length at 15 to 23 weeks' gestation. *J Ultrasound Med* 2009; 28: 49-53.
13. Jung E, Won HS, Lee PR, Kim A. Ultrasonographic measurement of fetal nasal bone length in the second trimester in Korean population. *Prenat Diagn* 2007; 27: 154-7.
14. Zelop CM, Milewski E, Brault K, Benn P, Borgida AF, Egan JF. Variation of fetal nasal bone length in second-trimester fetuses according to race and ethnicity. *J Ultrasound Med* 2005; 24: 1487-9.
15. Yalınkaya A, Güzel Aİ, Uysal E, Kangal K, Kaya Z. The fetal nose bone nomogram according to gestational weeks. *Perinatal Journal* 2009; 17: 100-3.
16. Odibo AO, Sehdev HM, Sproat L, Parra C, Odibo L, Dunn L, et al. Evaluating the efficiency of using second-trimester nasal bone hypoplasia as a single or a combined marker for fetal aneuploidy. *J Ultrasound Med* 2006; 25: 437-41.
17. Tran LT, Carr DB, Mitsumori LM, Uhrich SB, Shields LE. Second-trimester biparietal diameter/nasal bone length ratio is an independent predictor of trisomy 21. *J Ultrasound Med* 2005; 24: 805-10.

Turkish Demographic and Health Survey Results of Antenatal Care, Perinatal Fetal and Neonatal Evaluation With Respect to Prognosis

Derya Sivri Aydın¹, Murat Yayla²

¹*Istanbul Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, TR*

²*International Hospital, Kadın Hastalıkları ve Doğum Kliniği, İstanbul, TR*

Abstract

Objective: Turkey Demographic Health Surveys data, which was completed in 2008 was analyzed. Examination of the fetus and newborn outcome of pregnancies, use of antenatal care services and to evaluate the effect on the results of antenatal care services.

Methods: Turkey Demographic Health Surveys data, which was completed in 2008 by the Ministry of Health, Hacettepe University Institute of Population Studies and Macro International was analyzed.

Results: The results of the survey data and questioning the general population has been reached adjusting the following comments: 1) Only 78.4% of pregnancies ends with a live birth in Turkey 2) Pregnancies can not end live births consist of spontaneous abortions rate is 49%, induced abortions rate is 46% and stillbirths rate is 5%. 3) Receiving prenatal care in health care workers and health facility to perform the birth rate reached over 90% 4) Remarkable increase in cesarean section rates. 5) Although antenatal care services increased neonatal mortality reduction should be to question the quality of service became clear that this is not satisfactory.

Conclusion: Our country is trying to reach with the relevant health data, two points come to our attention. The first is the absence of a registry system in our country healthy for the fetus and newborn, and the second each year about 300 thousand babies died before birth or the neonatal period with the main responsibility for the quality of antenatal care services across the country, is that still inadequate. Solution to these problems, emphasis will be given again, recording systems and improving the quality of antenatal care services passes.

Keywords: Turkey, antenatal care, caesarean section rate.

Türkiye nüfus ve sağlık araştırması sonuçlarının antenatal bakım, fetal perinatal ve neonatal prognoz yönünden irdelenmesi

Amaç: İkinsekiz yılında tamamlanmış olan Türkiye Nüfus Sağlık Araştırmaları'na ait veriler ile gebeliklerin fetus ve yenidoğan akıbeti yönünden incelenmesi, antenatal bakım hizmetlerinden yararlanma ve antenatal bakım hizmetinin elde edilen sonuçlar üzerindeki etkisinin değerlendirilmesi.

Yöntem: Sağlık Bakanlığı, Hacettepe Üniversitesi Nüfus Etütleri Enstitüsü ve Macro International tarafından 2008 yılında tamamlanmış olan Türkiye Nüfus Sağlık Araştırmaları'na ait veriler incelendi.

Bulgular: Anket ve sorgulama verilerinin sonuçları toplum geneline uyarlandığında aşağıdaki yorumlara ulaşıldı: 1. Türkiye'de gebeliklerin sadece %78.4'ü canlı doğum ile sonlanmaktadır, 2. Canlı doğumla sonlanmayan gebeliklerin %49'u istemsiz düşüklükler, %46'sı istemli düşüklükler, %5'i ise ölü doğumlardan oluşmaktadır, 3. Sağlık personelinde doğum öncesi bakım alma ve doğumu sağlık kuruluşunda gerçekleştirme oranı %90'ların üzerine çıkmıştır, 4. Sezaryen oranlarındaki artış dikkat çekicidir. 5. Antenatal bakım hizmeti arttırdığı halde neonatal mortalitedeki azalmanın tatminkar olmaması bu hizmetin kalitesini sorgulamamız gerektiğini ortaya çıkartmıştır.

Sonuç: Ülkemiz ile ilgili sağlık verilerine ulaşmaya çalışırken iki nokta dikkatimizi çekmiştir. Bunlardan birincisi ülkemizde fetus ve yenidoğan ile ilgili sağlıklı kayıt sisteminin bulunmadığı, ikincisi ise her yıl doğumdan önce veya yenidoğan döneminde kaybedilen yaklaşık 300 bin bebeğin asıl sorumluluğunu taşıyan antenatal bakım hizmetlerinin ülke genelindeki kalitesinin hala yetersiz olduğudur. Bu sorunların çözümü, yine kayıt sistemlerine verilecek önem ve antenatal bakım hizmetlerinin kalitesinin yükseltilmesinden geçmektedir.

Anahtar Sözcükler: Türkiye, antenatal bakım, sezaryen oranı.

Introduction

The level of baby and child deaths generally reflects the level of health service and general living conditions in a society. Although these services and conditions are separated into two groups as prenatal and postnatal, they are the components forming a whole. It is an expected from a service given prenatally to affect also the postnatal period.¹

According to 2008 data of Turkish Demographic and Health Survey (TNSA), still-birth rate is 7/1000, early neonatal death rate is 11/1000, perinatal death rate is 19/10000 and death rate within first month after delivery is 13/1000. Among these deaths, 17% is stillbirth, 32% is neonatal death, 10% is postneonatal death and 41% is baby death. Also, the progress of baby mortality in the last decade is in the range of 29-17/1000. To express these rates in numerical way, we can say that we lose approximately 14000 babies in the first month after delivery every year and we lose 20000 - 25000 babies in the first year after delivery.

On the other hand, according to TNSA 2008 results, it was shown that 22 of each 100 pregnancies in Turkey did not result with viable birth in the last five years. In Turkey, according to the information that there were 1.262.333 deliveries in 20082, approximately 356.000 pregnancies were resulted with spontaneous abortion or stillbirth every year. By excluding 49% of abortions which are "induced abortions", we can estimate that approximately 180.000 of pregnancies are resulted with loss.

Our aim in this study is to analyze pregnancies in our country in terms of fetus, newborn and baby outcomes in parallel with Turkish Demographic and Health Survey and to emphasize positive and negative points.

Methods

The data of Turkish Demographic and Health Surveys (TNSA) completed in 2008 by Turkish Ministry of Health, Population Etudes

Institute of Hacettepe University and Macro International were analyzed.

1998, 2003 and 2008 Guides of Turkish Demographic and Health Surveys were used in order to reach the data related with pregnancies and their outcomes in Turkey. Approximately 10000 households and 7500 married women were interviewed by all three surveys and data were obtained with 5% error margin enabling us to generalize the society and these results were confirmed by next researches.

Results

Abortions

According to the 2008 data of Turkish Statistics Institute, there were 1.262.333 deliveries in 2008 in Turkey. This number constitutes approximately three fourths of all pregnancies. Short-term outcomes of pregnancies are given in Table 1.

Table 1. Gestational prognosis.*

TNSA	1993-1998	1998-2003	2003-2008
Induced abortion	14.5	11.3	10.0
Spontaneous abortion	8.7	10.0	10.5
Stillbirth	1.5	1.3	1.1
Live birth	75.3	77.4	78.4

* Rates are given as percentage.

As noticed, spontaneous abortion rate in 2008 is 10.5%. When the data of TNSA 2003 and TNSA 2008 are compared, it is seen that the rate of induced abortion decreases 11% and the rate of spontaneous abortion increases 5%. When all married women (age 15-49) are considered according to the data of last 5 years, the rate of women who had induced abortion is 22%, the rate of women who had spontaneous abortion is 20% and the rate of those with stillbirth is 4%. 6% of all married women had induced abortion, 8% of them had abortion more than once and less than 1% of them had pregnancy more than once which resulted with stillbirth.

The point standing out here is that the outcomes obtained from family planning methods for years are actually disputable. While 34% of women did not use any method before induced abortion, 22% of them used a modern contraceptive method (11% condom, 5% pills, 5% RIA) and 44% of them used traditional methods such as using calendar and withdrawal method. None-use of any method by 32% of women and use of withdrawal method by 22% of women during the first month after induced abortion emphasize the requirement of giving consultancy for family planning after induced abortion.

15% of pregnancies according to 1998 data, 11% of pregnancies according to 2003 data and 10% of pregnancies according to 2008 data are ended with induced abortion. As it is understood here, over 180.000 pregnancies are ended with induced abortion every year and it is a high rate when compared with general delivery number. The distribution of these induced abortion over gestational months are given in Table 2.

Table 2. Gestational months in induced abortions.*

TNSA	1998	2003	2008
1st month	68	73	67
2nd month	23	22	22
3+ month	9	5	11

*Rates are given as percentages.

Prenatal Care and Neonatal Postneonatal Mortality

When antenatal care and getting support for delivery are compared with mortality rates in TNSA 1998 data, a difference drawn attention in terms of neonatal mortality (neonatal mortality rate of those who got antenatal care was 23/1000 and it was 37/1000 for those who did not get antenatal care); and this was detected more clearly in postneonatal mortality (postneonatal mortality rate was 5/1000 for those

who got antenatal care and it was 58/1000 for those who did not get antenatal care). When the rates and outcomes of getting care compared to previous years are interpreted, a clear decrease is observed in mortality for those who get full care.¹ Existence of relationship between neonatal mortality and antenatal care services required to question antenatal care service and it is seen that TNSA 2003 and 2008 gave more detailed data for antenatal care services.

According to TNSA 2008 data, 90% of women took prenatal care from at least one physician (totally 92% of them from health personnel) during their last deliveries within last five years before the survey date. When TNSA-1998 and TNSA-2008 results are compared, the rate of getting prenatal care was increased from 68% to 92% (Table 5). This indicates approximately 75% decrease in the rate of women who did not get any prenatal care.

The rate of getting antenatal care is high in young women (93%), in those pregnant for their first children (98%), and those living in urban areas. Prenatal care is at the lowest rates in Northeast, Middle-east and Southeast Anatolia (73%, 76% and 82%, respectively).

Initiating prenatal care at the early periods of pregnancy is useful and effective on preventing pregnancy to result negatively. When 1998 and 2008 data in the Table are compared, it is seen that women are more aware of the importance of getting prenatal care. First visit median value which was 3.1 months in 1998 reduced to 2.8 months in 2003 and reduced to 2.2 months in 2008.

Table 3. Stillbirth rates during reproductive periods of married women.

TNSA	1993	1998	2003	2008
Total	5.7	5.0	4.0	4.0
1 stillbirth		4.3	3.5	3.5
2 stillbirths		0.5	0.3	0.4
3 and more stillbirths		0.2	0.2	0.1

Table 4. Stillbirth number per 100 pregnancies.

TNSA	1993	1998	2003	2008
	1.9	1.5	1.3	1.1

Gestational complications are the most important reasons for maternal deaths, early neonatal deaths and morbidity. Therefore, effective prenatal care for providing safe maternity depends on tests and measurements performed in order to determine possible complications during these controls. It is seen that 92% of women's blood pressure was measured who got prenatal care, 82% of them had urine test, 86% of them had blood analysis, 96% of them had ultrasonographic analysis at least one of their prenatal visits and 83% of them had weight measurement. It was also found that fundus pubis examination performed during prenatal care had a low rate (74%). 80% of pregnant women stated that they used iron supplements. As seen in Table 6, fundus pubis examination rate given in TNSA-2008 data increased significantly though it is still at the lowest rate compared to other examinations and measurements.

While the rate of delivery performed in a health organization was 78% according to the date of TNSA-2003, it was found as 90% throughout the country according to TNSA-2008. Women who got prenatal delivery four or

more times had 97% of their deliveries in a health organization. In case that prenatal care was not taken, the rate of performing delivery at home is 34%. While delivery rate in a health organization is 80% in rural areas, it is 94% in urban areas. The rate of deliveries performed in a health organization is above the country average in all regions except Eastern region (72%). Middle Anatolia region has the highest rate (98%) in terms of deliveries performed in a health organization followed by Western and Northern regions (96%).

Getting help from trained health personnel during delivery has a major importance in terms of preventing maternal deaths and neonatal deaths. While the rate of all deliveries within last five years performed by getting trained health personnel was 83% in TNSA-2003, it was 91% in TNSA 2008.

Delivery by Cesarean

Delivery by cesarean is quite common in Turkey. According to TNSA 2008 data, 37% of all deliveries done in the last five years were done by cesarean. The rate of delivery by cesarean increased largely (21%) according to TNSA-2003. Another point found significant in the data is that the rate of cesarean at first delivery increased more than 100% as to 1998. 45% of first deliveries were done by cesarean (Table 7). Cesarean is more common among women living in urban areas (42%) compared to

Table 5. The rates of getting antenatal care.*

	1998	2003	2008
**Getting antenatal care	68	81	92
*Getting antenatal care from physician	60	71	90
*Care before 6th month of pregnancy	60	71	87
*Median pregnancy duration at first visit	3.1 months	2.8 months	2.2 months
*Getting antenatal care more than four times	42	54	74
*In urban areas	?	64	80
*In rural areas	?	33	55

* Rates are given as percentage.

women living in rural areas (24%). Deliveries by cesarean are over 40% in all regions except Eastern Anatolia (16%). Cesarean rates increase as education and welfare levels increase.

Table 6. Rates of tests and measurements performed during prenatal care.*

	2003	2008
Blood pressure measurement	89	92
Fundus pubis examination	46	73
Ultrasonographic examination	90	96
Urine test	73	82
Blood test	77	86

* Rates are given as percentage.

Table 7. Rates of deliveries by cesarean.*

TNSA	1993	1998	2003	2008
The rate of delivery by cesarean	7	14	21	37
The rate of cesarean at first delivery		20	30	45

* Rates are given as percentage.

It is clear that getting antenatal care, performing delivery at a health organization and getting help from trained health personnel during delivery has a significant contribution on the decrease of the rates of perinatal, neonatal and postneonatal death though there is no direct explicative data in TNSA-2008. There is need for studies explaining relationship between these parameters and neonatal and postneonatal death rates in next TNSA.

Neonatal mortality decreased from 40/1000 to 13/1000 and postneonatal mortality decreased from 5/1000 to 4/1000 in last 30 years. Stillbirth and early neonatal death numbers and perinatal death rates are given in Table 8 for the five years before TNSA-2008 according to some basic demographic and socio-economical variables. When the rate 24/1000 given in TNSA-2003 is considered, it is seen that there is a decrease in perinatal death rate in last five years.

Table 8. Intervals of postnatal death rates according to years.*

	Neonatal mortality	Postneonatal mortality	Baby mortality
1978-1982	37-42	54-58	92-100
1983-1988	35-45	37-47	70-81
1988-1993	29-30	23-24	53-54
1993-1998	26	17	43
1998-2003	17	12	29
2003-2008	13	4	1

* Rates are given as percentage.

It is seen that perinatal death rate is quite high among women in 40-49 age group and women younger than 20 years old. There is a strong relationship between pregnancies occurring with short intervals and perinatal death rate. Perinatal death rates in pregnancies occurring in intervals shorter than fifteen months are two times higher than pregnancies occurring in intervals of 15-26 and 27-38 months. Perinatal deaths in urban areas are higher than rural areas. It is seen that the Western region has the highest perinatal death rate among all regions. This conflicting highness in perinatal death rate in Western region may caused by ending abnormal fetuses by establishing intrauterine diagnosis. Women with high education level have less perinatal death experience than educated women. Perinatal death rate in houses with low welfare level is higher than others. When considered according to regions, neonatal and postneonatal death rates are low in western regions while it is at the highest rates in Eastern and Southern regions.

Discussion

It is reported that approximate delivery in our country is 1.262.333 in a year.³ While the delivery number in İstanbul according to 1999 was 153.000, it increased to 212.000 in 2008 and baby death rate decreased from 25/1000 to 10.7/1000. Induced abortion rate was found as 29/1000 in Turkey while it was 42/1000 in İstanbul.

bul.⁵ Getting help from health personnel before and during delivery developed in recent years and 92% of women in Turkey got antenatal care service from health personnel while this rate increased to 97% for women living in Western regions. The rate of getting antenatal care was 68% in TNSA-2003 data and it increased to 92% according to 2008 data. The rate of delivery performed in a health organization was 78% according to TNSA-2003 data while it increased to 90% throughout the country according to TNSA-2008 data. Despite the increase in the rate of antenatal care, rate difference between urban and rural, east and west still continues. Getting help before and/or during delivery is still behind the desired level though it has a developing progress which has a positive effect on data related with baby death rates. It is emphasized that 65% of antenatal deaths and 78% of early neonatal deaths can be prevented under hospital conditions.⁶ In fact, the decrease obtained for postneonatal mortality in Turkey has a visible rate. However, it is hard to say same for neonatal mortality. When TNSA-2008 data are compared with 2003 data, it is seen that there is 67% decrease in postneonatal mortality while the decrease in neonatal mortality stayed at 24%. There may be two explanations that neonatal mortality rate does not change much by antenatal care and getting delivery help: either mortality has reached a level which can not be reduced anymore or the service given is insufficient. The quality of antenatal care service which reached the rate of 92% in Turkey should be questioned.

According to TNSA 2008 results, pregnancies below age 20 and above age 40, short delivery interval, low welfare level and low education level, high parity and low weighted baby birth affect mortality rate negatively. It is interesting that perinatal mortality rate is 20/1000 in urban areas while it is 17/1000 in rural areas. Among all regions, Western region has the highest perinatal death as 25/1000. While the rate of

getting antenatal care is 96% in western regions and it is 79% in eastern regions, these data seem inconsistent. It can be considered that this difference might be created by risks which may be brought by urban life (accident, bad habits, heavy work life etc.) and early diagnosis factor (early diagnosis of anomalies and abortion etc.) in care services.

Approximately one third of reasons of newborn mortalities develop depending on congenital malformation.⁷ As there is no comprehensive data about this issue in our country, the role of congenital malformation on fetal and neonatal mortalities can not completely be established. However, in order to prevent some of neonatal mortality, it is required to diagnose major malformations early and to end these pregnancies within legal and ethic limits. In other words, when antenatal care service is given completely, morbidity can be decreased and the situations which can not avoid mortality will be detected at early periods. It is important to detect in time those who especially live in rural areas and within risk group in terms of delivery and newborn and direct them to health organizations.

Considering the distribution of prenatal care services, more than 90% of pregnant population had prenatal care service at least once while more than 70% of pregnant had prenatal care four or more times. This service is at remarkable rates in cities and western regions. First application month in antenatal care decreased from 3.2 months to 2.2 months in the last 10 years.

It is observed that health organizations are preferred much more in first deliveries, in urban regions, and by those with high education and welfare level living in Middle Anatolia region. There are also some differences in terms of people helping delivery: the rate of deliveries helped by physicians are less than the rate of deliveries helped by nurses or midwives in east and southeast regions.

The rate of deliveries by cesarean increased to 37% among all deliveries. Cesarean rates increase together with maternal age, and in those living in urban areas and having high education and welfare levels.

Conclusion

Consequently, two points come to our attention trying to reach health data of our country. Firstly, there is no comprehensive registration system for fetuses and newborns, and secondly, the quality of antenatal care services is still low throughout the country while it is primarily responsible for 300.000 babies lost every year before delivery or at newborn period. The solution for these problems can be provided by creating comprehensive registration systems and increasing the quality of antenatal care services. In order to diagnose diseases and risky pregnancies early, proper diagnosis and correct registration system should be added into that solution list.

References

1. Yayla M, Şen C. Türkiye nüfus ve sağlık araştırması sonuçlarının fetal perinatal ve neonatal prognoz yönünden irdelenmesi. *Perinatoloji Dergisi* 2002; 10: 47-50.
2. Hacettepe Üniversitesi web portal. Türkiye Nüfus ve Sağlık Araştırması Sonuçları 2008. http://www.hips.hacettepe.edu.tr/tnsa2008/data/TNSA-2008_ana_Rapor-tr.pdf2008
3. Türkiye İstatistik Kurumu web portal. Türkiye İstatistik Kurumu 2008 Verileri. <http://www.tuik.gov.tr/PreHaberBultenleri.do?id=61642008>
4. Kale A, Akdeniz N, Retrospective analysis of 660 still-birth cases during ten years period. *Perinatal Journal* 2005; 13: 101-4.
5. Hacettepe Üniversitesi web portal. TNSA 2008'in sonuçları, bölge toplantısı-4. http://www.hips.hacettepe.edu.tr/tnsa2008/data/TNSA_2008_Sonuclar_Adana.pdf2009
6. Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, et al. Williams Obstetrics. 20. ed. Connecticut: Appleton&Lange; 1997; p. 5.
7. Incerpi MH, Miller DA, Samadi R, et al. Stillbirth evaluation: What tests are needed? *Am J Obstet Gynecol* 1998; 178: 1121-5.

Seroprevalence of Toxoplasmosis Among Pregnant Women in Kayseri

Tuba Kayman,¹ Mesut Kayman²

¹Kayseri Eğitim ve Araştırma Hastanesi, Mikrobiyoloji Laboratuvarı, Kayseri

²Kayseri Doğumevi ve Çocuk Hastalıkları Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Kayseri

Abstract

Objective: In the present study, we aimed to determine the seroprevalence among pregnant women at risk for toxoplasmosis in Kayseri and contribute to the management of toxoplasmosis in antenatal follow-up of pregnant women in Turkey.

Methods: Toxoplasma IgM antibodies were investigated in 1813 pregnant women, 46 (2.5%) of whom were detected to be positive. Toxoplasma IgG antibodies were investigated in 1676 pregnant women, 568 (33.9%) of whom were found to be positive. Regarding the age-related analysis of pregnant women, toxoplasma gondii IgG positivity was observed to increase with age.

Results: The results obtained in pregnant women aged between 16-45 years, who were referred to Kayseri Maternity Hospital from January 2006-December 2008, were examined retrospectively for toxoplasmosis. Levels of Toxoplasma gondii specific IgG and IgM were determined by microparticle EIA (AxSYM, Abbott, USA) technique.

Conclusion: Because of being seronegative for toxoplasma, more than 60% of pregnant women are at risk for toxoplasmosis. Toxoplasma serology and serological surveillance should be performed during obstetrical follow-up of all pregnant women. It is also of high importance to educate seronegative pregnant women about protection from infection.

Keywords: Pregnancy, seroprevalence, toxoplasmosis.

Kayseri'deki gebelerde Toksoplazmoz seroprevalansı

Amaç: Bu çalışmada, Kayseri bölgesinde toksoplazmoz açısından risk altındaki gebelerin seroprevalansının saptanması ve ülkemizde gebelerin antenatal takibinde toksoplazmoz yönetimine katkıda bulunmak amaçlanmıştır.

Yöntem: Ocak 2006-Aralık 2008 tarihleri arasında Kayseri Doğumevi'ne başvuran 16-45 yaş aralığındaki gebelerin sonuçları toksoplazmoz yönünden retrospektif olarak araştırılmıştır. Toksoplazma Ig G ve Toksoplazma Ig M değerleri mikropartikül EIA(AxSYM, Abbott, USA) yöntemiyle çalışılmıştır.

Bulgular: Toksoplazma IgM 1813 gebede çalışılmış, 46 (%2.5)'sında pozitiflik saptanmıştır. Toksoplazma IgG 1676 gebede çalışılmış, 568 (%33.9)'inde pozitiflik saptanmıştır. Gebeler yaş gruplarına göre incelendiğinde, toksoplazma IgG pozitifliğinin yaşla arttığı görülmüştür.

Sonuç: Gebelerin %60'dan fazlası seronegatif olduğundan toksoplazmoz açısından risk altındadır. Tüm gebelerin gebelik takibinde Toksoplazmoz serolojilerinin saptanması ve takibi gereklidir. Seronegatif gebelerin enfeksiyondan korunmaları için eğitim verilmesi önem taşımaktadır.

Anahtar Sözcükler: Gebelik, seroprevalans, toksoplazmoz.

Introduction

Toxoplasmosis is a worldwide multi-system infection caused by the protozoan parasite *Toxoplasma gondii*, which can infect all vertebrates.¹

The infection follows a 90% asymptomatic course in healthy adults and leaves a life-long immunity. The transmission of the infection to human occurs mainly through raw or rare meat infected with the tissue cysts, as well as raw

foods and water contaminated with oocytes.² Trophozoites are known to play a major role in the transmission from infected mother to child. Additionally, the infection may also be transmitted through blood transfusion and tissue transplantation from a donor with toxoplasmosis.^{3,4}

Toxoplasmosis during pregnancy can lead to not only preterm birth, stillbirth or miscarriage but congenital toxoplasmosis with potentially severe consequences.¹

Congenital toxoplasmosis occurs as a consequence of placental transmission of the parasite to the fetus after a primary or recurrent parasitemia during pregnancy. In pregnant women with untreated acute infections, the risk of congenital fetal infection was detected to be 25% in the first trimester, 54% in the second trimester, and 65% in the third trimester.⁵ This rate exceeds 90% during the last two weeks of pregnancy. Due to increased placental surface area and placental blood flow, the risk of infection increases in direct proportion to the duration of the pregnancy; however, the rate of occurrence of severe sequelae is directly proportional to the infection in early gestational weeks.^{6,2}

90% of infants with congenital toxoplasmosis are asymptomatic during neonatal period. In time, serious conditions such as cataract, glaucoma, hepatitis, pneumonia, myocarditis, myocyte and mental retardation in addition to hydrocephaly characterized by a classic triad of symptomatic congenital toxoplasmosis, intracranial calcifications and chorioretinitis are observed. To prevent these life-threatening sequelae which have a significant effect on the quality of life, antenatal treatment as well as screening and follow-up pregnant women for toxoplasmosis are of great importance.⁷

In the present study, we aimed to determine seroprevalence among pregnant women at risk for toxoplasmosis and contribute to the management of toxoplasmosis in antenatal follow-up of pregnant women.

Methods

The results obtained in pregnant women aged between 15-45 years who were referred to Kayseri Maternity Hospital between January 2006 and December 2008, were examined retrospectively for toxoplasmosis. Levels of *Toxoplasma gondii*-specific IgG and IgM that are routine antenatal screening tests in asymptomatic pregnant women, were determined using microparticle EIA (AxSYM, Abbott, USA) technique. IgM index values of ≥ 0.600 were defined as positive, values between 0-0.499 as negative and those between 0.500- 0.599 as equivocal. IgG index values of ≥ 3.00 IU/ml were defined as positive, values between 0-1.99 IU/ml as negative and those between 2.00-2.99 IU/ml as equivocal. Of over 3000 registered patients in the hospital database, those aged between 15-45 years were selected and recurrent cases were excluded. Data from 1813 patients were collected for *Toxoplasma* IgM and data from 1676 patients for *Toxoplasma* IgG and entered into SPSS version 17.0 for Windows for the statistical analysis.

Results

Toxoplasma IgM antibodies were investigated in 1813 pregnant women, 46 (2.5%) of whom were detected to be positive. In 16 (0.9%) patients, IgM values were found to be between 0.5 and 0.599 and defined as equivocal. *Toxoplasma* IgM antibodies were reinvestigated in these patients three weeks later, which however, was not included in the study. In 36 of 46 pregnant women who were positive for *Toxoplasma* IgM antibodies, *Toxoplasma* IgG was also found to be positive.

Since only IgM is evaluated in acute infection assays in several pregnancy follow-up studies, the number of patients in whom *Toxoplasma* IgG antibodies were investigated was smaller than that in whom *Toxoplasma* IgM antibodies were measured and *Toxoplasma*

IgG antibodies were investigated in 1676 cases, 568 (33.9%) of whom were detected to be positive.

When 1676 pregnant women in whom Toxoplasma IgG antibodies were investigated, were evaluated after being divided into 3 age groups, IgG positivity was determined as 28.1% in those aged between 15-25 years, 35.2% in those between 26-35 years, increasing up to 46.7% in those between 36-45 years (Table 1).

Table 1. Toxoplasma gondii IgG positivity according to age in pregnant women.

Age	The number of pregnant women	Positive
15-25	622	175 (28.1%)
26-35	859	302 (35.2%)
36-45	195	91 (46.7%)
Total	1676	568 (33.9%)

Discussion

Seroprevalence of toxoplasmosis varies throughout the world depending on age, socioeconomic conditions, eating and hygiene habits, climate and geographic location. The infection is more common in societies with low socioeconomic level, lack of hygiene during feeding and frequent contact with soil and cats. The seroprevalence increases with age.⁸

Table 2 and 3 present the rates of Toxoplasma gondii IgG positivity obtained

from studies on pregnant women and women of reproductive age in Turkey and in the world.

The rates of Toxoplasma IgG gondii positivity in pregnant women and women of reproductive age vary across countries and regions throughout the world. Similarly, regional differences manifest themselves in rates for our country.

In the present study, seroprevalence of toxoplasmosis was found to be 33.9% in pregnant women, which is consistent with other results obtained in Turkey. However, this rate is lower when compared to those obtained in particularly Hatay and Şanlıurfa, which is considered to be caused by cultural differences in eating habits.

When 1676 pregnant women who were screened for Toxoplasma IgG antibodies, were evaluated after being divided into 3 groups according to their ages, it was observed that the seropositivity increased in direct proportion to the age.

In the present study, because of being seronegative for toxoplasma, more than 60% of pregnant women are at risk for toxoplasmosis. These pregnant women should be given education about the transmission of toxoplasmosis and ways to protect against the infection.

In the present study, IgM positivity was found to be 2.5%. However, false-positive results may be obtained in IgM testing and the

Table 2. Toxoplasma IgG positivity (%) in women of reproductive age.

In other countries(9)		In Turkey	
Spain, 2000	43.8	Ankara, 2002 ¹⁰	31.7
Indonesia, 2003	60	Şanlıurfa, 2007 ¹¹	69.5
Netherlands, 2004	35.2	Isparta, 2008 ¹²	25.2
Brasil, 2004	51.2	Malatya, 2008 ¹³	32.5
USA, 2007	11		
Switzerland, 2007	8.2		
Iran, 2007	63.9		
Greece, 2008	21.2		
Romania, 2008	57.6		

Table 3. Toxoplasma IgG positivity (%) in pregnant women

In other countries		In Turkey	
Argentina, 2003 ⁹	48.7	Ankara, 2001(14)	38.1
Britain, 2005 ⁹	9.1	Sivas, 2002(15)	46.6
Brasil, 2006 ⁹	61.1	Şanlıurfa, 2004(16)	60.4
Switzerland, 2006 ⁹	35	Afyonkarahisar, 2004(17)	30.7
Mexico, 2006 ⁶	6.1	Aydın, 2005(18)	30.1
Morocco, 2007 ⁹	50.6	Hatay, 2007(19)	52.1
India, 2007 ⁹	45	Van, 2009(20)	36
Poland, 2008 ²¹	55.5	Kocaeli, 2009(22)	48.3
Colombia, 2008 ²³	45.8	Kayseri (This study)	33.9
France, 2009 ²⁴	43.8		
Albania, 2009 ²⁵	48.6		
China, 2009 ²⁶	10.6		

positivity may continue for nearly a year. Therefore, IgM positivity does not always predict an acute infection whereas IgM negativity does not exclude the infection because of the fact that IgM positivity may not be detected at the onset of the infection or when tested at the late stage of pregnancy, the result might have become negative although the mother had been infected during the pregnancy. For this reason, IgG avidity test in addition to IgM and IgG antibody testing should be performed in the first trimester of pregnancy. High avidity results, particularly, are suggested to represent the acquisition of the infection at least 3-5 months ago.^{15,27}

Since the diagnosis of toxoplasmosis is established when a pregnant women who is seronegative for toxoplasmosis prior to the pregnancy becomes positive during the pregnancy, a basal serologic test should be performed before a planned pregnancy.

Conclusion

Toxoplasmosis is of critical importance because of leading to serious complications when acquired as primary infection during pregnancy. In examinations of women of reproductive age before and after pregnancy, serologic tests for toxoplasmosis should be per-

formed, which should be followed by required treatments and follow-up according to the obtained result. Pregnant women who have not been infected with *t. gondii*, should be educated about protection methods.

References

1. Töre O. Toxoplasma gondii. In: Topçu AW, Söyletir G (Ed). İnfeksiyon Hastalıkları. Nobel Tıp Kitabevleri-1996; 525-32.
2. Remington JS, Desmonts G. Toxoplasmosis. In: Remington JS, Klein JO (Ed). Infectious Diseases of the Fetus and Newborn Infant. WB Saunders-1990; 89-174.
3. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. *Clin Microbiol Infect* 2002; 8(10): 634-40.
4. Saygı G. Temel Tıbbi Parazitoloji. Sivas-Esnaf Ofset Matbaacılık: 1998; 71-7.
5. Desmonts G, Couvreur J. Congenital toxoplasmosis. A prospective study of 378 pregnancies. *N Engl J Med* 1974; 290(20): 1110-6.
6. Alvarado-Esquivel C, Sifuentes-Alvarez A, Narro-Duarte SG. Seroepidemiology of Toxoplasma gondii infection in pregnant women in a public hospital in northern Mexico. *BMC Infect Dis* 2006; 6: 113.
7. Madazlı R. Toxoplasma. In: Madazlı R (Ed). Fetusa Etkili Enfeksiyon Hastalıkları. Scala Yayıncılık-2000; 213-61.
8. Kılıçturgay K, Göral G, Gökırmak F ve ark. Bursa yöresinde Toxoplasma antikor araştırılması. *T Parazitol Derg* 1989; 13(3-4): 23-32.
9. Pappas G, Roussos N, Falagas ME. Toxoplasmosis snapshots: global status of Toxoplasma gondii. *Int J Parasitol* 2009; 39(12): 1385-94.

10. Özkan S, Maral I, Bumin MA. Gölbaşı'nda birinci basamak sağlık hizmetlerinde çalışan ebe, hemşire. *T Klin Jineköl Obst* 2002; 12: 258-61.
11. Tekay F, Özbek E. Çiğ köftenin yaygın tüketildiği Şanlıurfa ilinde Toxoplasma gondii seroprevalansı. *T Parazitöl Derg* 2007; 31(3): 176-9.
12. Güneş H, Kaya S, Çetin ES, Taş T, Demirci M. Reprodükatif çağıdaki kadınlarda toksoplazmosis seroprevalansı. *S.D.Ü. Tıp Fak Derg* 2008; 15(2): 21-4.
13. Pala M, Karaman Ü, Atambay M, Daldal N. Hiç gebe olmayan kadınlarda (18-25 yaş grubu). *İnönü Üniv Tıp Fak Derg* 2008; 15(4): 257-60.
14. Saraçoğlu F, Şahin İ. Gebe popülasyonunda Toksoplazma prevalansı ve duyarlı gebelerde serolojik dönüşüm oranı. *T Klin Jineköl Obst* 2001; 11: 326-8.
15. Duran B, Toktamış A, Erden Ö, Demirel Y, Mamık BA, Çetin M. Doğum öncesi bakımda tartışmalı bir konu: TORCH taraması. *Cumhuriyet Üniv Tıp Fak Derg* 2002; 24(4): 185-90.
16. Harma M, Harma M, Gungen N, Demir N. Toxoplasmosis in pregnant women in Sanliurfa, South Eastern Anatolia City, Turkey. *J Egypt Soc Parasitol* 2004; 34(2): 519-25.
17. Yilmazer M, Altındış M, Cevrioglu S, Fenkci V, Aktepe O, Sirthan E. Afyon bölgesinde yaşayan gebe kadınlarda Toksoplazma, Sitomegalovirus, Rubella, Hepatit B, Hepatit C seropozitiflik oranları. *Kocatepe Tıp Derg* 2004; 5: 43-9.
18. Ertug S, Okyay P, Turmen M, Yuksel H. Seroprevalence and risk factors for Toxoplasma infection among pregnant women in Aydin province, Turkey. *BMC Public Health* 2005; 5: 66.
19. Ocak S, Zeteroglu S, Ozer C, Dolapcioglu K, Gungoren A. Seroprevalence of Toxoplasma gondii. *Scand J Infect Dis* 2007; 39(3): 231-4.
20. Efe Ş, Kurdoğlu Z, Korkmaz G. Van yöresindeki gebelerde sitomegalovirus, rubella ve toksoplazma antikorlarının seroprevalansı. *Van Tıp Derg* 2009; 16(1): 6-9.
21. Marcinek P, Nowakowska D, Szaflik K, Spiewak E, Malafiej E, Wilczynski J. Analysis of complications during pregnancy in women with serological features of acute toxoplasmosis or acute parvovirus. *Gineköl Pol* 2008; 79(3): 186-91.
22. Tamer GS, Dundar D, Caliskan E. Seroprevalence of Toxoplasma gondii, rubella and cytomegalovirus among pregnant women in western region of Turkey. *Clin Invest Med* 2009; 32(1): E43-7.
23. Rosso F, Les JT, Agudelo A et al. Prevalence of infection with Toxoplasma gondii among pregnant women in Cali, Colombia, South America. *Am J Trop Med* 2008; 78(3): 504-8.
24. Berger F, Goulet V, Le Strat Y, Desenclos JC. Toxoplasmosis among pregnant women in France: Risk factors and change of prevalence between 1995 and 2003. *Rev Epidemiol Sante Publique* 2009; 57(4): 241-8.
25. Maggi P, Volpe A, Carito V et al. Surveillance of toxoplasmosis in pregnant women in Albania. *New Microbiol* 2009; 32(1): 89-92 .
26. Liu Q, Wei F, Gao S et al. Toxoplasma gondii infection in pregnant women in China. *Trans R Soc Trop Med Hyg* 2009; 103(2): 162-6.
27. Montoya JG, Liesenfeld O, Kinney S, Press C, Remington JS. Vidas test for avidity of Toxoplasma-specific immunoglobulin G for confirmatory testing of pregnant women. *J Clin Microbiol* 2002; 40(7): 2504-8.
28. Yazar S, Yaman O, Şahin İ. Toxoplasma gondii seropozitif gebelerde IgG-avidite sonuçlarının değerlendirilmesi. *T Parazitöl Derg* 2005; 29(4):221-3.

The Impact of Placental Location on Early Fetal Growth

Rahime Nida Ergin, Murat Yayla

International Hospital Kadın Doğum Kliniği, Kadın Hastalıkları ve Doğum, İstanbul, TR

Abstract

Objective: In this study it is aimed to determine the impact of the placental placement of the fetus on the biometric parameters assessed during 11-14 th gestational weeks in singleton pregnancies.

Methods: According to the study including criteria, 1615 pregnant women were evaluated. The median maternal age was 29.0 ± 4.6 years. 54% of pregnant women were nulliparous and the rest 46% was multiparous. Median pregnancy number was 1.0 ± 1.06 . Median sonographic pregnancy week was 12.57 ± 0.63 weeks. Fetal placental placement was 50.2% anterior, 41% posterior, 5.3% lateral and 3.5% fundus. The analysis done separately for 11 0-11 6; 12 0-12 6; 13 0 -13 6 week intervals showed no statistically significant difference between groups of placental locations in terms of in terms of biometric measurements.

Results: We retrospectively assessed spontaneous pregnancies screened between 2004 – 2010 having no uterine or anatomical abnormalities, systemic disease and family history of genetic diseases. Prenatal ultrasound biometry parameters like biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL) and crown-rump length (CRL) were evaluated. Fetuses were divided into groups according to placental location and whether groups differ in terms of biometric values was investigated. The effect of placement of the placenta on biometric values were evaluated separately for 11 0-11 6; 12 0-12 6; 13 0 -13 6 week intervals.

Conclusion: There is no significant effect of the placental placement of the fetus on the biometric parameters assessed during 11-14 th gestational weeks in singleton pregnancies.

Keywords: Placenta, biometry, fetus, ultrasonography, localization, growth.

Plasental Yerleşimin Erken Fetal Büyümeye Etkisi

Amaç: Gebeliğin 11-14.haftasındaki tekil gebeliklerde elde edilen biyometrik parametrelere plasenta yerleşiminin etkisinin var olup olmadığının araştırılması amaçlanmıştır.

Yöntem: Birinci trimester taraması 2004 - 2010 yılları arasında yapılmış olan, sistemik hastalığı veya ailevi genetik hastalığı olmayan, spontan gebelik öyküsü bulunan, uterin veya fetal anatomik anomali saptanmayan gebeler retrospektif olarak değerlendirmeye alındı. Biparietal Çap (BPD), Baş çevresi (HC), Karın çevresi (AC), Femur uzunluğu (FL) ve Baş-Popo Mesafesi (CRL) gibi prenatal ultrasonografik biyometri parametreler değerlendirmeye alındı. Fetüsler plasenta yerleşimine göre gruplara ayrılarak gruplar arasında biyometrik değerler açısından farklılık olup olmadığı araştırıldı. Biyometrik değerlere plasenta yerleşiminin etkisi 11 0-11 6; 12 0-12 6; 13 0 -13 6. haftalar için ayrı ayrı değerlendirildi.

Bulgular: Çalışma kriterlerine uygun 1615 gebe değerlendirmeye dahil edildi. Ortanca anne yaşı 29.0 ± 4.6 yıl saptandı. Ortanca gebelik sayısı 1.0 ± 1.06 bulundu. Gebelerin %54'ü nullipar ve %46'sı multipar idi. CRL'ye göre ortanca sonografik gebelik haftası 12.57 ± 0.63 hafta idi. Fetüslerin plasenta yerleşimi %50.2 anterior, %41 posterior, %5.3 lateral ve %3.5 fundus idi. Yapılan değerlendirmede 11 0-11 6; 12 0-12 6; 13 0 -13 6. haftalar için gruplar plasenta yerleşimine göre parametreler karşılaştırıldığında anlamlı fark saptanmadı.

Sonuç: 11-14.hafta tekil gebeliklerde prenatal ultrasonografik değerlendirme ile elde biyometri parametrelerine plasenta yerleşiminin etkisi mevcut değildir.

Anahtar Sözcükler: Plasenta, biyometri, fetus, ultrasonografi, lokalizasyon, büyüme.

Introduction

In the present clinical practice, ultrasonographic fetal examination and evaluation of chromosomopathy is performed in the first trimester. This approach helps early detection of probable malformations of fetus and guiding to treatment if possible, thus it serves reduction in the general health expenses. Therefore, the determination of the standard measurement values obtained in the first trimester ultrasonography and their alterations related to maternal, fetal or environmental factors is important for the assessment of these measurements.¹⁻³

In this study we aimed to determine the impact of the placental location of the fetus on the biometric parameters assessed during 11-14 th gestational weeks in singleton pregnancies.

Methods

We retrospectively assessed spontaneous pregnancies screened between 2004–2010 without the uterine or anatomical abnormalities, systemic disease and family history of genetic diseases. Prenatal ultrasound biometry parameters like biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and crown-rump length (CRL) were evaluated for the ones matching inclusion and exclusion criteria above. As previously described in the literature, fetuses were divided into groups according to their placental location, namely as anterior if the main part of placenta lies close to the anterior wall of the uterus; posterior if the main part of placenta lies close to posterior

wall; lateral if the main part of placenta lies close to lateral walls and fundal if the main part of placenta lies at the fundus.⁴ Whether groups differed in terms of biometric values was investigated. The effect of location of the placenta on biometric values were evaluated separately for 11 0-11 6; 12 0-12 6; 13 0 -13 6 week intervals.

Anova test was used for the evaluation of mean values between groups. The statistical analyses were done with SPSS for Windows version 14.0 (SPSS Inc, Chicago, IL, ABD). The value of $p < 0.05$ was considered as statistically significant.

Results

According to the study including criteria, 1615 pregnant women were evaluated among 1725 pregnancies evaluated in the first trimester. The median maternal age was 29.0 ± 4.6 years. Median pregnancy number was 1.0 ± 1.06 . Fifty-four percent of pregnant women were nulliparous and the rest 46% was multiparous. Median sonographic pregnancy week was 12.57 ± 0.63 weeks.

Fetal placental location was anterior in 50.2%, posterior in 41%, lateral in 5.3% and fundus in 3.5%. The comparisons of the groups according to the demographics like median maternal age, median number of pregnancies and median gestational week are shown in the table 1. Among groups there was found no statistical significant differences in the median maternal age, median number of pregnancies and median gestational week. The comparative analysis of the biometric measurements of the

Table 1. Demographics of groups based on placenta location (Median \pm S.D).

Placenta Location	Anterior	Posterior	Lateral	Fundus	p
Maternal Age	29.0 \pm 4.6	29.0 \pm 4.7	30.0 \pm 3.8	30.0 \pm 3.9	0.184
Number of Pregnancies	1.0 \pm 0.92	1.0 \pm 1.21	1.5 \pm 0.67	1.0 \pm 0.50	0.126
USG gestational week	12.57 \pm 0.64	12.57 \pm 0.63	12.57 \pm 0.55	12.50 \pm 0.56	0.604

groups done separately for 11 0-11 6; 12 0-12 6; 13 0-13 6 week intervals is shown in the Table 2. The analysis showed no statistically significant differences between groups of placental locations in terms of biometric measurements.

Discussion

It is important to know the normal patterns of all measurements done in the first trimester ultrasonographic scanning and their alterations according to the maternal and fetal factors in order to assess these measurements in the proper way.^{1,3} Thus, in our study the effect of placental location on the ultrasonographic measurements done in the first trimester was studied retrospectively. Limited numbers of studies on this subject are present in the literature.

Woods et al suggested that placental location had no effect on the babies' weights in a study which evaluated 940 term babies at birth.⁵ In another study of Woods et al, they suggested no effect of placental location on both newborn babies' weights and newborn babies' heights.⁶ In that study, also it was suggested that babies with fundal location of placenta had larger head circumference in comparison with the other locations. Distinctively our study

included earlier intrauterine period and it suggested no effect of placental location on the measurements of first trimester ultrasonography including biparietal diameter, head circumference, abdominal circumference and crown-rump length. In our study, mean biparietal diameters of the fetuses with fundal location of placenta were smaller compared to the other sites in the 11th and 12th gestational weeks but this difference was not statistically significant. Though Woods' finding related to the larger head circumference of term babies with fundal placenta was not confirmed in our study for an earlier life period of fetus, whether this difference occurs later in fetal life should be sought by further comparative studies done throughout the whole period of fetal development. In the study of Stožkov et al which followed 289 pregnancies after determination placental location in the third trimester, it was suggested that location of placenta had no effect on birth weights and heights of the babies.⁷

Our study includes the measurements which are done in the first trimester. Other three studies included the measurements of the term babies done after birth. However, in all studies the measurements of fetuses or babies were not affected by the location of placenta (except

Table 2. Fetal biometrics according to the localization of placenta.

Gestational Week		Biparietal Diameter (mm)	Head Circumference (mm)	Abdominal Circumference (mm)	Femur Length (mm)	CRL (mm)
11 0-11 6 Week	Anterior (n=187)	18.31±1.71	69.88±5.69	55.03±4.56	5.54±1.05	53.75±4.37
	Posterior (n=153)	18.18±1.72	69.61±6.09	54.79±4.68	5.56±1.10	53.67±4.39
	Lateral (n=11)	18.36±1.50	68.80±5.43	55.60±3.50	6.08±1.12	52.00±3.82
	Fundus (n=11)	17.45±1.21	67.27±4.56	52.81±4.83	5.47±0.91	50.82±3.84
12 0-12 6 Week	Anterior (n=439)	21.11±2.00	79.56±6.19	63.67±5.67	7.54±1.53	63.14±4.93
	Posterior (n=359)	21.16±1.93	79.37±6.54	63.88±5.81	7.49±1.58	63.10±4.62
	Lateral (n=60)	20.98±1.68	79.17±6.44	63.92±6.25	7.10±1.23	62.12±3.63
	Fundus (n=38)	20.16±1.75	76.81±5.51	61.85±5.69	6.94±1.37	61.50±4.57
13 0-13 6 Week	Anterior (n=168)	24.38±2.09	90.88±7.14	74.21±6.29	10.09±1.85	74.13±5.45
	Posterior (n=137)	24.09±2.23	89.87±7.10	73.10±6.23	9.83±1.93	73.68±5.81
	Lateral (n=13)	24.12±1.42	88.73±6.67	72.55±6.63	10.30±1.46	73.46±4.71
	Fundus (n=7)	24.28±1.60	91.00±6.32	72.71±9.76	10.17±2.14	73.28±3.94

larger head circumference of the babies with fundal placenta in the study of Woods). As a result, it can be concluded that the measurements related to the growth of the fetuses are not affected by the location of placenta starting from the first trimester to birth. During the development of placenta, chorion villuses migrate to the locations where the blood flow is appropriate and this phenomena is explained by the tropotrophism theory.^{8,9} It seems that unless blood flow to the placenta is not appropriate, the first localization of placenta does not have an important effect on the fetal growth. In addition, in case of placenta previa the birth weights are lower and this situation is rather attributed to preterm birth.¹⁰ In another study, though there was found no difference in terms of birth weight and chest circumference in births of 28-32th weeks, there was significant difference in the births after 33th weeks in cases of placenta previa.¹¹ Also it has been shown that the restriction of intrauterine growth of preterm newborns without anomalies is frequently symmetrical and is mainly attributed to abnormal uteroplacental or fetoplacental blood flow.¹²

Conclusion

As a conclusion, blood flow to the placenta rather than placental location seems to be more important for the fetal growth. Our present preliminary study suggests that the location of placenta does not affect the fetal growth in terms of biometric parameters. More detailed studies on this subject might be helpful for further understanding.

References

1. Gardosi J, Chang A, Kalyan B, Sahota D, Symonds EM. Customised antenatal growth charts. *Lancet* 1992 ; 1; 339: 283-7.
2. Mongelli M, Gardosi J. Longitudinal study of fetal growth in subgroups of a low-risk population. *Ultrasound Obstet Gynecol* 1995; 6: 340-4.
3. Pang MW, Leung TN, Sahota DS, Lau TK, Chang AM. Customizing fetal biometric charts. *Ultrasound Obstet Gynecol* 2003; 22(3): 271-6.
4. Kofinas AD, Penry M, Greiss FC Jr, Meis PJ, Nelson LH. The effect of placental location on uterine artery flow velocity waveforms. *Am J Obstet Gynecol* 1988; 159(6): 1504-8.
5. Woods DL, Malan AF. The site of umbilical cord insertion and birth weight. *Br J Obstet Gynaecol* 1978; 85(5): 332-3.
6. Woods DL, Malan AF, Heese Hde V, Leader LR, van Schalkwyk DJ. The site of placental insertion and fetal growth. *S Afr Med J* 1980 ;28;57(26):1087-8.
7. Stoikov S, Bogdanova A. The dependence of fetal weight and fetal length at birth on the site of placental attachment. *Akush Ginekol (Sofia)* 1993; 32(2): 14-6.
8. Monie IW. Velamentous insertion of the cord in early pregnancy. *Am J Obstet Gynecol* 1965; 93: 276-81.
9. Hasegawa J, Matsuoka R, Ichizuka K, Sekizawa A, Okai T. Umbilical cord insertion site in early gestation and development of placenta. *J Perinat Med* 2009; 37(5): 481-5.
10. Ananth CV, Demissie K, Smulian JC, Vintzileos AM. Relationship among placenta previa, fetal growth restriction, and preterm delivery: a population-based study. *Obstet Gynecol* 2001; 98(2): 299-306.
11. Li YN. Effect of placenta previa on fetal growth and development. *Zhonghua Fu Chan Ke Za Zhi* 1992; 27(3): 141-3.
12. Salafia CM, Minior VK, Pezzullo JC, Popek EJ, Rosenkrantz TS, Vintzileos AM. Intrauterine growth restriction in infants of less than thirty-two weeks' gestation: associated placental pathologic features. *Am J Obstet Gynecol* 1995; 173(4): 1049-57.

Fetal Goiter in the Absence of Maternal Thyroid Disease: A Case Report

Arif Güngören¹, Kenan Dolapçioğlu¹, Ali Ulvi Hakverdi¹, Ali Balcı², İsmail Güzelmansur³

¹Mustafa Kemal Üniversitesi, Kadın Hastalıkları ve Doğum, Hatay, TR

²Mustafa Kemal Üniversitesi, Radyoloji, Hatay, TR

³Özel Mozaik Hastanesi, Radyoloji, Hatay, TR

Abstract

Objective: Most believe that it is important to be able to recognize and treat the fetal hypothyroidism in order to get the most out of growth and intellectual development in affected fetuses.

Case: A case has been introduced dealing with a woman contracted with fetal goiter that was identified by ultrasonography at 30 weeks of gestation. In Doppler examinations, it was realized that the thyroid gland was highly vascularized and diffusely enlarged. Under these circumstances, fetal goiter may only have something to do with fetal hypothyroidism. The patient was offered to get through amniotic fluid sampling via amniocentesis or cord blood sampling via cordocentesis, but she rejected the performance of these procedures.

Conclusion: Our priority is, whenever the situation permits, to trust in the ultrasonographic measurement of goitre size and color doppler signal, since it is of vital importance to be able to recognize and observe the fetal goiter based on ultrasound and Doppler examination.

Keywords: Fetal goiter, ultrasonography, prenatal diagnosis.

Maternal tiroid hastalığı yokluğunda fetal guatr: bir olgu sunumu

Amaç: Etkilenen fetusların çoğunda fiziksel ve zihinsel gelişme geriliklerine yol açabildiğinden, fetal hipotiroidizmin tanınması ve tedavi edilmesinin oldukça önemli olduğu düşünülmektedir.

Olgu: Bu yazıda 30 haftalık iken ultrasonografi ile tespit edilmiş bir fetal guatr olgusu sunulmuştur. Hastanın tiroid hastalığı öyküsü mevcut değildi ve tiroid otoantikolarının negatif oluşu da dahil tüm tiroid fonksiyon testleri normaldi. Dopler ultrasonografide diffüz olarak büyümüş ve yüksek oranda kanlanan tiroid bezi izlendi. Bu durumda fetal guatrın sadece fetal hipotiroidizme bağlı olabileceği düşünüldü. Kesin tanı için amniosentez veya kordosentez yaptırması önerilen hasta bunu kabul etmedi.

Sonuç: Bu durumda önceliğimiz, klinik durumun tanı ve takibinin öneminden dolayı, ultrason bulguları ve dopler ölçümlerine güvenmek oldu.

Anahtar Sözcükler: Fetal guatr, ultrasonografi, prenatal tanı.

Introduction

Thyroids disorders are common endocrine disorders encountered during the perinatal period. It is very difficult to identify and diagnose the fetal goiter, while maternal thyroid

abnormalities can be easily diagnosed applying maternal serum testing.¹ Different biochemical defects in thyroid hormone synthesis, or maternal autoimmune thyroid disease might cause fetal goiter.² Goiter might have association with fetal hypothyroidism or hyperthyroidism. Many

authors, on this issue, believe that fetal thyroid function has to be determined for beginning the early treatment.³ Weiner et al reported that they diagnosed the fetal goiter by means of pre-natal sonography for the first time in 1980.⁴ A very large goiter inside uterus might cause polyhydramnios because of esophageal and tracheal compression, and distocia as well, leading to hyperextension in the neck.⁵

Case

The patient was a 28 year-old primigravida who referred to our hospital at 30 weeks of gestation for having ultrasound examination. The ultrasound examination indicated a large homogeneous mass in the anterior aspect of the fetal neck. The mother was married to a second-degree cousin. There was no family history of thyroid or autoimmune diseases and no maternal history of a past thyroid disease. There was no known guatrogens including iodine or thyroid medications. Following ultrasonography a wide, symmetrical bilobated thyroidal mass and a mild polyhydramnios, compressing the fetal trachea in the anterior portion of the neck, were detected. The mass appeared highly vascularized during the Power Doppler examination (Figure 2). After birth, color Doppler examination showed a diffusely enlarged thyroid gland (Figure 3).

Fetal heart rate was about 220 beats/min. No other anomaly was noted in the fetus. Fetal growth and movements were normal. Maternal serum thyroid function test results were normal. Ultrasound of the maternal thyroid was usual. We suggested amniotic fluid sampling via amniocentesis or cord blood sampling via cordocentesis to the mother but she refused the suggestion. The patient was advised for bed rest to avoid premature labor. We did not attempt to obtain fetal blood to confirm fetal hypothyroidism, however we proposed intra-amniotic l-thyroxin injections for to start early treatment.



Figure 1. Symmetrical bilobated thyroidal mass.



Figure 2. Highly vascularized mass.

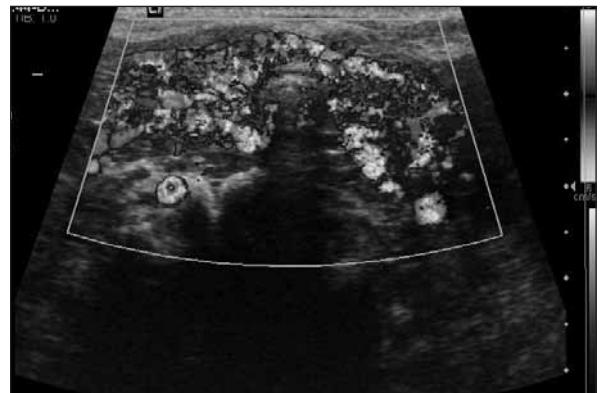


Figure 3. After birth, color Doppler examination showed a diffusely enlarged thyroid gland.

Both parents did not allow this procedure too. We tried to rely on ultrasonographic measurement of goiter size and color Doppler signal

when applicable. At 36 weeks of gestation the patient is hospitalized for premature rupture of membranes and delivered a male newborn, weighing 2600 g by caesarean section because of the narrow pelvis. His Apgar scores were 6 at 1 min and 7 at 5 min. Although a soft bilobated goiter was present, neonatal airway obstruction was not observed and resuscitation was not needed. He had no problem in respiratory adaptation postnatally. Measurement of TSH and iodothyronines in the cord blood confirmed the diagnosis of primary hypothyroidism. Thyroid hormone therapy commenced on the first day of life with a daily oral dose of 50 µg levothyroxine. The weight, height and psychomotor development of the child were normal at 6 months of age.

Discussion

Incidence rate of congenital hypothyroidism is one out of 4000 live birth, causing the mental retardation that can most commonly be treated.⁶ It is very seldom (one out of 4000) to encounter fetal goitrous hypothyroidism, constituting only 10 to 15% of all congenital hypothyroidism cases.⁷ Because of the development of ultrasound technology, reports on the investigations of fetal goiter, despite being a rare incidence, has gradually been increasing.⁸

A large goiter may cause hyperextension of the fetal neck, resulting in malpresentation and complicating labor and delivery. Following the birth, the trachea may be blocked by goiter, which may cause asphyxia and death. During delivery, pediatric anesthesia and pediatric ear, nose and throat consultants have to be present in an adjoining theater with intubation and bronchoscopy equipment set up. Neonatal screening programs have successfully been used for diagnosing congenital hypothyroidism shortly after birth, and the prognosis for normal development has dramatically improved with earlier postnatal treatment. However some

infants exposed to congenital hypothyroidism have encountered difficulties and delays in neuromotor, perceptual and language abilities, despite early postnatal therapy. Therefore, antenatal treatment of congenital hypothyroidism has to be taken into account and given priority.⁹

Pathological cases, including the thyroid gland, can easily be distinguished from cases with other neck lesions detected at ultrasound. The differential considerations of fetal goiter should include all anomalies of the anterior and anterolateral nuchal region, including teratomas, thyroglossal duct cysts, cystic hygromas, lymphangiomas/hemangiomas, branchial cleft cysts and other developmental cystic lesions.¹⁰ These lesions frequently appear as fluid-filled cystic masses. This finding enables the differentiation of the neck lesions from thyroid gland masses.¹¹

Amniotic fluid concentrations of TSH accurately reflect fetal serum levels, but Bruner and Dellinger consider cord blood measurements more reliable, thus render evaluation through amniocentesis doubtful. Fetal thyroid function can be accurately assessed by fetal blood sampling, but this procedure is riskier with about 1 % fetal demise in experienced hands.¹²

We reported this situation to the family members but the parents rejected the suggestion of performing amniocentesis and/or fetal blood sampling. We observed the size and fetal development of the fetal goiter until delivery, using the ultrasound and Doppler examination.

Conclusion

As a result, ultrasound and Doppler examination are of vital importance in recognition and observation of fetal goiter. Therefore, mental retardation and other developmental (evolutional) disorders could be prevented in the incidence where early diagnosis and treatment have already been utilized.

References

1. Singh PK, Parwin CA, Gronowski AM. Establishment of reference intervals for markers of fetal thyroid status in amniotic fluid. *J Clin Endocrinol Metab* 2003; 88: 4175-9.
2. Polk DH. Diagnosis and management of altered fetal thyroid status. *Clin Perinatol* 1994; 21: 647-62.
3. Perrotin F, Sembely-Taveau C, Haddad G, Lyonais C, Lansac J, Body G. Prenatal diagnosis and early in utero management of fetal dysmorphogenetic goiter. *Eur J Obstet Gynecol Reprod Biol* 2001; 94: 309-14.
4. Weiner S, Scharf JI, Bolognese RJ, Librizzi RJ. Antenatal diagnosis and treatment of a fetal goiter. *J Reprod Med* 1980; 24: 39-42.
5. Davidson KM, Richards S, Schatz DA, Fisher DA. Successful in utero treatment of fetal goiter and hypothyroidism. *N Engl J Med* 1991; 324: 543-6.
6. Delange F. Neonatal screening for congenital hypothyroidism: Results and perspectives. *Horm Res* 1997; 48: 51-61.
7. Fisher DA. Fetal thyroid function: Diagnosis and management of fetal thyroid disorders. *Clin Obstet Gynecol* 1997; 40: 16-31.
8. Meideros-Neto GA, Stanbury JB. Inherited Disorders of the Thyroid System. Boca Raton-CRC Pres: 1994: 1-218.
9. Morine M, Takede T, Minekawa R, Sugiyama T, Wasada K, Mizutani T et al. Antenatal diagnosis and treatment of a case of fetal goitrous hypothyroidism associated with high-output cardiac failure. *Ultrasound Obstet Gynecol* 2002; 19: 506-9.
10. Volumenie JL, Polak M, Guibourdenche J, Oury JF, Vuillard E, Sibony O et al. Management of fetal goiters: a case report of 11 cases in a single perinatal unit. *Prenat Diagn* 2000; 20: 799-806.
11. Farrell PT. Prenatal diagnosis and intrapartum management of neck masses causing airway obstruction. *Paediatr Anaesth* 2004; 14: 48-52.
12. Simsek M, Mendilcioglu I, Mihci E, Karagüzel G, Taksın O. Prenatal diagnosis and early treatment of fetal goitrous hypothyroidism and treatment results with two year follow up. *J Matern Fetal Neonatal Med* 2007; 20: 263-5.

Successful Maternal and Fetal Outcome in a Pregnancy With Type V Takayasu's Arteritis

Hüseyin Levent Keskin¹, Olcay Turgut¹, Işık Üstüner¹, Sinan Tan², Ayşe Filiz Avcı¹

¹Atatürk Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum, Ankara, TR

²Atatürk Eğitim ve Araştırma Hastanesi, Radyoloji, Ankara, TR

Abstract

Objective: Takayasu's Arteritis is a rare idiopathic, chronic inflammatory disease causing intimal proliferation. Preexisting hypertension in pregnant women with Takayasu's Arteritis may pose risks for both the mother and the fetus. The aim of this study is to report a pregnant woman with Type V Takayasu's Arteritis and pregnancy outcomes.

Case: The 34-year-old woman with the diagnosis of Takayasu's Arteritis for 6 years had stopped her Takayasu's Arteritis medications without having asked her doctor at the time she learned of her pregnancy. After an uncontrolled pregnancy, when she presented to our clinic without any antenatal followup, no complications of pregnancy were determined in her first examination. After vaginal delivery she was discharged on the second postpartum day with no maternal or fetal complications.

Conclusion: Although there was no problem due to Takayasu's Arteritis in our patient and she experienced a pregnancy without any problems, pregnant women with Takayasu's Arteritis should be regarded and followed up as high risk pregnancies due to the risk of hypertension.

Keywords: Takayasu's arteritis, pregnancy.

Tip V Takayasu Arteritli bir gebelikte başarılı maternal ve fetal Sonuç

Amaç: Takayasu Arteriti, idiyopatik, nadir görülen, kronik, intimal proliferasyon gösteren inflamatuvar bir hastalıktır. Gebeliği olan Takayasu arteritli kadınlarda ise mevcut olan hipertansiyon, anne ve fetus açısından riske neden olabilmektedir. Bu yazıda amacımız Tip V Takayasu arterit hastası bir gebeyi ve gebelik sonuçlarını sunmaktır.

Olgu: Otuz dört yaşında, 6 senedir Takayasu Arteriti tanısı olan olgu, gebe olduğunu öğrendiği anda doktora başvurmadan kendi kararı ile Takayasu Arteriti için aldığı ilaçları almayı bırakmış. Antenatal takibi hiç yapılmamış olan olguda takipsiz bir gebelik süreci sonrasında kliniğimize başvurduğu ilk muayenesinde gebelik komplikasyonu saptanmamıştır. Vajinal yolla doğum yapan, travay ve postpartum süreçte maternal ve fetal herhangi bir komplikasyon gelişmeyen hasta postpartum 2.günde taburcu edilmiştir.

Sonuç: Olgumuzda Takayasu Arteritine bağlı bir problem olmamasına ve sorunsuz bir gebelik geçirmiş olmasına rağmen, Takayasu arterit hastası olan gebeler hipertansiyon riski nedeniyle yüksek riskli gebelik olarak kabul edilmeli ve takipleri buna uygun yapılmalıdır.

Anahtar Sözcükler: Takayasu arteriti, gebelik.

Introduction

Takayasu's Arteritis (TA) is a rare, idiopathic chronic inflammatory disease causing intimal proliferation.¹ Its annual incidence is 2.6/million new cases and the prevalence is 2.6-6.4/million.² The disease affects women more com-

monly than men and the mean age at which the disease appears is in the second decade. Its etiology is still not clearly understood.³ It is a rare polyarteritis characterized by fibrosis in the renal and pulmonary arteries, more commonly affecting the branches of the aortic arch.⁴ The

symptoms and signs appear as a consequence of obliterative vascular changes. Coldness and pain in the upper extremities, claudication in the lower extremities due to narrowing of the iliac artery, and intraabdominal and cerebral ischemia due to disease involvement of the mesenteric and cervical arteries may occur. Retinopathy may cause visual loss.⁴ High blood pressure levels are present in 33-50% of patients with TA and this hypertension especially occurs in patients with renal artery involvement and stenosis.^{2,3,5} Preexisting hypertension in pregnant women with TA may pose risks for the mother and the fetus.^{6,8} Herein we report a pregnant woman with Type V TA and the consequences of pregnancy.

Case

Takayasu's Arteritis (TA) that had been present for 6 years was determined in the history of a 34-year-old woman with gravida 3 and parity 2, who had presented to our clinic due to the commencing of uterine contractions at the 39+3 weeks' gestation of her pregnancy according to her last menstruation date. The patient was poorly compliant with her medication and had stopped taking her drugs that had been prescribed for TA (Prednisolone 15 mg/day, Pentoxifyllin 400 mg/day, Acetylsalicylic acid 100 mg/day) at the sixth week of her pregnancy without having informed any doctor. She had not been to any medical facility for the antenatal follow-up.

On her physical examination, blood pressure could not be measured on either of the upper extremities. The radial pulse could not be obtained bilaterally on either of the upper extremities, while the brachial arterial pulses were palpated as weak. On her bilaterally lower extremity arteries, the arteria femoralis, tibialis posterior and dorsalis pedis, pulses were palpated weak.

On the obstetric examination, the cervical opening was 5 cm, effacement 60%, the fetus was on vertex presentation, the level was -2. On the contraction stress test, she had regular contractions as high as 70-80 mmHg and the test was negative. On ultrasonographic examination, there was a fetus consistent with 38-39 weeks of gestational age, with head presentation and estimated weight of 3230 grams. The amniotic index was 165 mm. On Doppler examination, the umbilical artery Systole/Diastole ratio was determined as 2.22. On laboratory evaluations, complete urine analysis, complete blood count, biochemical tests including liver function tests and coagulation parameters were all found to be normal.

The angiography of thoracoabdominal aorta and its branches performed about 1 year ago had shown widespread and severe stenosis. The graphy had shown stenosis in the truncus brachiocephalicus (1), bilaterally subclavian arteries (2,5), right a.carotis interna (3), left a.carotis interna (4), bilaterally upper extremity arteries (arrows). The graphies had shown also generalized stenosis and contour irregularities on the descending thoracic aorta and in the area of the infrarenal abdominal aorta, especially involved bilateral renal arteries and superior mesenteric artery, stenotic aortic bifurcation and common iliac arteries (6) (Figure 1). According to these physical examination and angiographic findings the patient was determined as Type V TA.

The patient's status underwent the consultations of the cardiology, cardiovascular surgery, internal medicine and rheumatology clinics, and no contraindications for vaginal birth were determined through a multidisciplinary approach. After 4 hours of active labor, a 3100 g. girl baby with an Apgar score of 7/9 was delivered through vaginal birth. No peripartum maternal or fetal complications developed. No anomaly was detected in the fetus. The patient was discharged on the second postpartum day.



Figure 1. 34-year-old woman with Type V Takayasu's arteritis. Oblique angiography shows generalized severe stenosis in the truncus brachiocephalicus (1), bilaterally subclavian arteries (2,5), right a.carotis interna (3), left a.carotis interna (4), bilaterally upper extremity arteries (arrows), and infrarenal abdominal aorta (6).

Discussion

Takayasu's Arteritis, which was first defined by the Japanese ophthalmologist Takayasu, is a chronic inflammatory disease of unknown etiology which affects the aorta and the large branches.² Takayasu's Arteritis has a large distribution with a high incidence, especially in Japan, East and South Asia, and India. Although its etiology still not clearly understood, autoimmunity is accused.³

TA is classified into 6 types anatomically and pathologically.^{9,10} Type I involves only the

branches of the aortic arch. Type IIa involves the aorta only at its ascending portion and/or at the aortic arch. The branches of the aortic arch may be involved as well. The rest of the aorta is not affected. Type IIb affects the descending thoracic aorta with or without involvement of the ascending aorta or the aortic arch with its branches. The abdominal aorta is not involved. Type III is concomitant involvement of the descending thoracic aorta, the abdominal aorta, and/or the renal arteries. The ascending aorta and the aortic arch and its branches are not involved. Type IV involves only the abdominal aorta and/or the renal arteries. Type V is a generalized type, with combined features of the other types.

Our patient was classified as Type V, due to physical examination and angiography findings of widespread contour irregularities on the arcus aorta, descending thoracic aorta and abdominal aorta, in addition to diffuse involvement of the renal artery, superior mesenteric artery and iliac arteries bilaterally (Figure 1).

The clinical patterns of TA differ at the acute and chronic periods. In the acute period, systemic symptoms prevail, while in the chronic period, insidious ischemic-destructive signs are more prevalent. These signs appear together with stenosis at a rate of 85%, dilatation at a rate of 2%, and stenosis and dilatation at a rate of 13%.²

Asymmetrically decreased peripheral pressure is determined in most of the patients. In approximately all of the patients, the measured blood pressure difference on symmetrical extremities is found to be higher than 10 mmHg.^{2,6} The evaluation of hypertension should be carefully performed on patients with TA, because peripheral blood pressure may be determined to be significantly lower than its actual value due to involvement of the aortic arch. Ideally, the central blood pressure should be measured using an aortic transducer.

Preexisting hypertension in pregnant women with TA may pose risks for the mother and the fetus.^{3,7,8,11} In our patient, however,

peripheral blood pressure could not be measured due to stenosis constituted by arteritis. Nevertheless, an invasive procedure, or a central catheter was not applied to her since the patient gave vaginal birth.

Gasch et al. reported the rate of pregnancy-induced hypertension/preeclampsia as 39% in their study of 137 pregnant women. Furthermore, they stated that although heart failure had developed in 5 of their cases, no maternal deaths had occurred.¹¹

In the evaluation of 115 cases from different centers with regard to the problems in the fetus due to ischemic and destructive reasons, the abortus rate was 15.6%, the premature birth rate was 9.5%, and the intrauterine growth retardation rate was 17%, and neonatal death was reported in only 1 case.^{3,5,7,8}

The rate of caesarean section was 26%. Twenty of the caesarian indications were maternal causes and 17 of these were maternal hypertension/preeclampsia and other vascular diseases.^{3,5,7,8}

There are some case reports on this subject in the Turkish medical literature. In 2 of the case reports, the birth facilitated through caesarean section.^{12,13} In the first case with high arterial blood pressure values and with the development of a superimposed preeclampsia, the indication of cesarean section was fetal distress,¹² while in the second case with normal blood pressure values all throughout her pregnancy, the cesarean indication was not clearly stated and the presence of TA singly was regarded as a maternal medical indication.¹³

In this case report, the woman did not undergo routine antenatal follow up. When the woman presented to our hospital at the term of her pregnancy, there were no pathological findings on the physical examination except non-palpable arterial pulsations of the peripheral arteries. Although she stopped the medical treatment of TA during her pregnancy, her pregnancy continued till the term and she did not present with any complications of pregnancy.

Conclusion

In conclusion, pregnancy per se does not appear to exacerbate the disease, but management of hypertension is essential for a successful maternal and fetal outcome. The pregnant women with TA should be regarded and followed-up as high risk pregnancies due to the risk of hypertension.

References

1. Kraemer B, Abele H, Hahn M, Rajab T, Kraemer E, Wallweiner D et al. A successful pregnancy in a patient with Takayasu's arteritis. *Hypertens Pregnancy* 2008; 27: 247-52.
2. Hall S, Barr W, Lie JT, Stanson AW, Kazmier FJ, Hunder GG. Takayasu arteritis. A study of 32 North American patients. *Medicine* 1985; 64: 89-99.
3. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M. Takayasu arteritis. *Ann Intern Med* 1994; 120: 919-29.
4. Ishikawa K, Matsuura S. Occlusive thromboangiopathy (Takayasu's disease) and pregnancy. *Am J Cardiol* 1982; 50: 1293-9.
5. Castellote E, Romero R, Bonet J, Torguet P, Callejas JM, Caralps A. Takayasu's arteritis as a cause of renovascular hypertension in a non-Asian population. *J Hum Hypertens* 1995; 9: 841-5.
6. Aso T, Abe S, Yaguchi T. Clinical gynecologic features of pregnancy in Takayasu arteritis. *Heart Vessels* 1992; 7: 125-32.
7. Sharma BK, Jain S, Vasistha K. Outcome of pregnancy in Takayasu arteritis. *Int J Cardiol* 2000; 75: 159-62.
8. Wong V, Wang R. Pregnancy and Takayasu's arteritis. *Am J Med* 1982; 75: 597-601.
9. Moriwaki R, Noda M, Yajima M, Sharma BK, Numano F. Clinical manifestations of Takayasu arteritis in India and Japan: new classification of angiographic findings. *Angiology* 1997; 48: 369-79.
10. Natri MV, Baptista LP, Baroni RH, Blasbalg R, de Avila LF, Leite CC et al. Gadolinium-enhanced three-dimensional MR angiography of Takayasu arteritis. *Radiographics* 2004; 24: 773-86.
11. Gasch O, Vidaller A, Pujol R. Takayasu arteritis and pregnancy from the point of view of the internist. *J Rheumatol* 2009; 36: 1554-5.
12. Bombacı E, Fidan G, Ekti Y, Çevik B, Çolakoglu S. Takayasu arteriti olan gebede spinal anestezi ile sezeryan seksiyonu. *Zeynep Kamil Tıp Bülteni* 2008; 39: 67-9.
13. Usta T, Özdemir B, Ateş U, Doğan Ö, Sidal B. Maternal Takayasu arteritli gebenin izlemi. *Vakıf Gureba Eğitim ve Araştırma Hastanesi Dergisi* 2006; 4: 121-3.

Isolated Fetal Endocardial Fibroelastosis Diagnosed and Terminated at 22 Weeks of Gestation: A Case Report

İnci Kahyaoğlu¹, Serkan Kahyaoğlu¹, Hatice Sut², Şahin Önen³, Leyla Mollamahmutoğlu¹

¹Zekai Tabir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi, Ankara, TR

²Trakya Üniversitesi Tıp Fakültesi Sağlık Bilimleri Enstitüsü, Edirne, TR

³Sağlık Bakanlığı Kızıltepe Devlet Hastanesi, Mardin, TR

Abstract

Objective: We present a case of diffuse endocardial fibroelastosis diagnosed at 22 weeks of gestation. The classification and clinical approach to fetal cardiomyopathies based on this syndrome will also be discussed.

Case: A healthy 22 year old primigravid woman had an uneventful pregnancy until the ultrasonographic examination at 22 weeks of gestation. Fetal echocardiographic evaluation revealed a dilated and hypotonic left ventricle with diffuse hyperechogenic endometrial lining. Left ventricular endocardium was thickened with accumulation of layers of collagen and elastin. Pathological confirmation of the diagnosis could not be made because parents refused autopsy examination.

Conclusion: Endocardial fibroelastosis is a rare disease and sporadically diagnosed during antenatal period. Sonographic criteria include a dilated left ventricle with poor contractility and hyperechogenic bright thickening of endocardial surface. When diagnosed, it should be wise to terminate the affected pregnancy since the prognosis is poor if it's detected before fetus is viable.

Keywords: Endocardial fibroelastosis; cardiac; pregnancy termination.

Yirmiikinci gebelik haftasında tanı konan ve termine edilen nadir bir izole endokardiyal fibroelastoz vakası: Bir olgu sunumu

Amaç: Yirmiikinci gebelik haftasında tanı konulan bir diffüz endokardiyal fibroelastoz vakasını sunuyoruz. Bu sendrom üzerinden fetal kardiyomiyopatilerin sınıflandırması ve klinik yaklaşım da tartışılacaktır.

Olgu: Sağlıklı 22 yaşındaki primigravid bir kadın 22. gebelik haftasındaki ultrason muayenesine kadar sorunsuz bir gebelik geçirmekteydi. Fetal ekokardiyografik değerlendirmede, diffüz hiperekojen endokardiyal çizgilenme ile birlikte olan dilate ve hipotonik sol ventrikül görüldü. Sol ventrikül endokardiyumu kollajen ve elastin tabaklarının birikimi ile kalınlaşmıştı. Aile postmortem incelemeyi reddettiği için tanının patolojik konfirmasyonu yapılamadı.

Sonuç: Endokardiyal fibroelastozis antenatal dönemde sporadik olarak tanı konulan nadir bir hastalıktır. Sonografik kriterler kötü kontraktileli sol ventrikül ve hiperekojen parlak kalınlaşmış endokardiyal yüzeyi içerir. Tanı konduğunda, hastalığın prognozu kötü olduğundan dolayı, fetüs viabilite kazanmadan etkilenmiş gebeliğin termine edilmesi akıllıca olacaktır.

Anahtar Sözcükler: Endokardiyal fibroelastozis; kardiyak; gebelik terminasyonu.

Introduction

Endocardial fibroelastosis (EFE) is a rare cardiac disorder characterized by diffuse proliferation of elastin and collagen fibers within the endocardium which mainly affects the left ventricle.¹ This mainly leads to decreased compliance and stroke volume. It has been classified as primary and secondary forms according to whether a structural cardiac anomaly is present such as aortic stenosis, coarctation or anomalies at the origin of left coronary artery or pulmonary trunk.² In the absence of these anomalies, it's described as primary disease. But most authors consider EFE as a secondary reactive process set off in the endocardium by stress on the myocardium.³ We present a case of diffuse endocardial fibroelastosis diagnosed at 22 weeks of gestation. The classification and clinical approach to fetal cardiomyopathies based on this syndrome will also be discussed.

Case

A healthy 22 year old primigravid woman had an uneventful pregnancy until the ultrasonographic examination at 22 weeks of gestation. Her past obstetrical and gynecologic history was unremarkable. Fetal echocardiographic evaluation revealed a dilated and hypotonic left

ventricle with diffuse hyperechogenic endocardial lining (Figure 1,2). Ultrasonographic examination of the fetus revealed normal aortic and mitral valve diameters and decreased aortic peak systolic velocity and mitral blood flow measurements were determined by doppler ultrasonography investigation. No associated cardiac or systemic anomalies were found on sonography. Parvovirus, coxackievirus infections and genetic or metabolic disorders were excluded. A presumptive diagnosis of EFE was made. Parents were told about the condition of the fetus and they elected to terminate the pregnancy. A male fetus compatible with 22 weeks of gestation with no other dysmorphic features was submitted to autopsy examination but parents refused it. Any other major abnormalities of the fetus was not found at postpartum examination.

Discussion

Cardiomyopathies (CM), account for 8% to 11% of the cardiovascular diagnoses detected prenatally.⁴ CM is diagnosed in 3% of newborns with cardiovascular disease.⁵ Single gen disorders (Noonan syndrome, metabolic disorders familial CM, congenitale myotonic dystrophy, X-linked myotubular myopathy), mitochondrial disorders, chromosome abnormalities and α



Figure 1. Transverse ultrasonographic view of fetal thorax demonstrating diffuse endocardial thickening with hyperechogenicity.



Figure 2. Lateral ultrasonographic view of fetal thorax demonstrating diffuse endocardial thickening with hyperechogenicity.

thalassemia are intrinsic and familial causes of primary CM with recurrence risk. Extrinsic causes of primary CM necessitates the investigation of fetal myocardial dysfunction, maternal hematologic indices and serological workup, amniocentesis if needed and invasive fetal sampling to assess for anemia, thrombocytopenia, high specific IgM titers, viral cultures, and polymerase chain reaction for the specific infectious agent.^{6,7}

Secondary CM includes cardiac causes, high output states, altered ventricular filling and altered ventricular afterload disorders. Diastolic dysfunction is associated with the greatest risk of mortality. Left and right ventricular end-diastolic diameters and wall thickness can be measured with M-mode tracings or 2-dimensional images (8,9). In normal fetuses semilunar and atrioventricular valve peak flow velocities gradually increases during pregnancy. Mitral and tricuspid valves have greater peak A velocity values than peak E velocity values throughout pregnancy. Diastolic dysfunction is considered when at least two of the following parameters are identified: Abnormal E/A ratio through mitral or tricuspid valve inflow (<2 SD below the mean for gestational age), increased duration of isovolumic relaxation time IVRT (>2 SD above the mean for gestational age), increased a-wave reversal in the inferior vena cava or hepatic vein (>20 cm/s) or a biphasic rather than triphasic flow pattern, and the presence of umbilical venous pulsations. Fetal echocardiography with a general fetal anatomic ultrasonographic scan and maternal laboratory investigations to establish the pathogenesis and exclude potentially treatable conditions should be evaluated during fetal CM investigation.¹⁰

The Tei index is a useful, new, noninvasive Doppler index of combined systolic and diastolic function calculated IVRT plus isovolumic contraction time (IVCT) divided by ejection time (ET). The Tei index readily provides early detection of diminished myocardial function, particularly ventricular dysfunction.¹¹

Endocardial fibroelastosis is a rare disorder of newborns accounting for no more than 1-4% of total congenital heart diseases.^{3,12} Around 80%

of patients present with congestive heart failure within the first year of life.¹³ Also one third of patients with clinically diagnosed EFE dies of congenital heart failure during the first 2 years of life. Late deaths occur in the group of patients with clinically resolved EFE.⁴

Classically, it has been classified into primary and secondary forms according to whether a structural cardiac anomaly is present since it was first proposed in 1960's. Recently it has been proposed that this was a nonspecific response to many stressors of myocardium such as congenital malformations of vessels and valves, viral agents affecting myocardium e.g. parvovirus, coxsackievirus, or genetic disorders, mitochondrial cardiomyopathies and

metabolic disorders. According to this thinking, diffuse intimal fibroelastic thickening of muscular arteries in response to chronic hypertension shares the same mechanism with EFE. When the heart is thought as a kind of modified vascular artery, its response to chronic stress will be the endocardial thickening which corresponds to intima of vessels.¹⁴ Endocardial smooth muscle cells which are normally few in number are seen to proliferate, transform into fibroblasts and produce both collagen and elastin under myocardial stress.

This fibroelastic reaction seems to occur during fetal development and growth, continuing after birth and throughout early infancy. The reason why this occurs more frequently in that life period is because of greater growth potential of cells at this period. Intestinal hyperechogenicities were also proposed as response to various fetal insults such as infection, hypoxia, vascular disease supporting the 'response to stress' theory.¹⁵

During the fetal development of EFE, echocardiographic appearance initially demonstrates left ventricular dilatation and hypocontractility with hyperechogenic thickening of endocardial surface as seen in this case. As the gestational age advances, the left ventricular cavity decreases in size, there's a progressive left ventricular wall hypertrophy and an increase in the hyperechogenicity of endocardial surface.¹⁶

A direct association between the thickness of endocardium and time of onset of myocardial stress was proposed.

Sonographic criteria include a dilated left ventricle with poor contractility and hyperechogenic bright thickening of endocardial surface.¹ According to this, presented case fulfills the both criteria. In differential diagnosis, causes of intracardiac echogenic focus should be included, most importantly Trisomy 21 and 13 which usually have other morphologic abnormalities.

Since there are controversies related to causes and majority of cases are sporadic as the presented case, a risk population to screen has not been proposed. In the literature, cases reported so far were diagnosed in the second and third trimester, the earliest one being diagnosed at 14 weeks of gestation. Time of diagnosis may be related to the severity of insult and the response of insulted tissue besides the duration of insult meaning under a severe stress, reaction of the tissue can be more prominent leading to early diagnosis.

Conclusion

EFE is a rare disease which sporadically diagnosed during antenatal period. Serial ultrasonographic evaluation is needed since it's a progressive condition which has a spectrum of findings. It should always be remembered that EFE is a response to a disease state rather than being a disease itself. Presence of hypocontractility and hyperechogenic endocardium necessitates excluding fetal echocardiography and congenital heart diseases. Since it's a progressive lesion, it has a spectrum of endocardial changes ranging from microscopic thickening to gross changes. When performing screening sonography, this should be kept in mind and special attention should be given to heart even if the previous scan is normal. When diagnosed, it should be wise to terminate the affected pregnancy since the prognosis is poor if it's detected before fetus is viable. If not, remaining antenatal period should be under the control of a pediatric cardiologist and an experienced perinatologist.

References

1. Tannouri F, Rypens F, Peny M, Noel JC, Donner C, Struyven J, Avni F. Fetal endocardial fibroelastosis: Ultrasonographic findings in two cases. *J Ultrasound Med* 1998; 17: 63-6.
2. Rustica MA, Benettoni A, Bussani R, Maieron A, Mandruzatto G. Early fetal endocardial fibroelastosis and critical aortic stenosis: a case report. *Ultrasound Obstet Gynecol* 1995; 5: 202-5.
3. Brandenburg RO, Chazov E, Cherian G, Falase AO, Grosgeat Y, Kawai C et al. Report of the WHO/ISCF task force on definition and classification of cardiomyopathies. *Circulation* 1981; 64: 437A-438A.
4. Allan LD, Crawford DC, Anderson RH et al. Spectrum of congenital heart disease detected echocardiographically in prenatal life. *Br Heart J* 1985; 54: 523-6.
5. Benson LN, Wilson GJ, Freedom RM. Myocardial disorders. In: Freedom RM, Benson L, Smallhorn JF (Ed). *Neonatal Heart Disease*. Springer-Verlag-1992: 693-722.
6. Bennet P, Nicolini U. Fetal infections. In: Fisk NM, Moise KJ (Ed). *Fetal Therapy: Invasive and Transplacental*. Cambridge University Press-1997: 92-116.
7. Wagner HR. Cardiac disease in congenital infections. *Clin Perinatol* 1981; 8: 481-97.
8. Hornberger LK, Sanders SP, Rein AJT et al. Left heart obstructive lesions and left ventricular growth in the midtrimester fetus: a longitudinal study. *Circulation* 1995; 92: 1531-8.
9. Tan J, Silverman NH, Hoffman JIE et al. Cardiac dimensions determined by cross-sectional echocardiography in the normal human fetus from 18 weeks to term. *Am J Cardiol* 1992; 70: 1459-67.
10. Pedra SR, Smallhorn JF, Ryan G, Chitayat D, Taylor GP, Khan R, Abdoell M, Hornberger LK. Fetal cardiomyopathies: pathogenic mechanisms, hemodynamic findings, and clinical outcome. *Circulation* 2002; 106(5): 585-91.
11. Ichizuka K, Matsuoka R, Hasegawa J, Shirato N, Jimbo M, Otsuki K et al. The Tei index for evaluation of fetal myocardial performance in sick fetuses. *Early Hum Dev* 2005; 81: 273-9.
12. Mitchell SC, Froelich LA, Banas JS, Jr, Gilkerson MR. An epidemiologic assessment of primary endocardial fibroelastosis. *Am J Cardiology* 1966; 18: 859-66.
13. Ino, T, Benson LN, Freedom RM, Rowe RD. Natural history and prognostic risk factors in endocardial fibroelastosis. *The American Journal of Cardiology* 1988; 62: 431-4.
14. Newbould MJ, Armstrong GR, Barson AJ. Endocardial fibroelastosis in infants with hydrops fetalis. *J Clin Pathol* 1991; 44: 576-9.
15. Lurie PR. Endocardial fibroelastosis is not a disease. *The American Journal of Cardiology* 1988; 62: 468-70.
16. Yagel S, Silverman NH, Genbruch U, Cohen SM. Diseases of myocardium, endocardium and pericardium during fetal life. In: Zielinsky P (Ed). *Fetal Cardiology*. Taylor and Francis-2003; 283.

PERINATAL JOURNAL

Volume 18 / Issue 3 / December 2010

Contents

Letter to the Editor	Toxoplasma Scanning During Pregnancy Ercüment Müngen	69
Research Articles	Nomogram of Fetal Cisterna Magna Width at 15-24th Gestational Weeks Resul Arisoy, Murat Yayla	72
	The Ratio of Biparietal Diameter to Nasal Bone Length Resul Arisoy, Nida Ergin, Murat Yayla, Gökhan Göynümer	79
	Turkey Demographic and Health Survey Results of Antenatal Care, Perinatal Fetal and Neonatal Evaluation With Respect to Prognosis Derya Sivri Aydın, Murat Yayla	85
	Seroprevalence of Toxoplasmosis Among Pregnant Women in Kayseri Tuba Kayman, Mesut Kayman	92
	The Impact of Placental Location on Early Fetal Growth Rahime Nida Ergin, Murat Yayla	97
Case Reports	Fetal Goiter in the Absence of Maternal Thyroid Disease: A Case Report Arif Güngören, Kenan Dolapçioğlu, Ali Ulvi Hakverdi, Ali Balcı, İsmail Güzelmansur	101
	Successful Maternal and Fetal Outcome in a Pregnancy With Type V Takayasu's Arteritis Hüseyin Levent Keskin, Olcay Turgut, Işık Üstüner, Sinan Tan, Ayşe Filiz Avşar	105
	Isolated Fetal Endocardial Fibroelastosis Diagnosed and Terminated at 22 Weeks of Gestation: A Case Report İnci Kahyaoğlu, Serkan Kahyaoğlu, Hatice Sut, Şahin Önen, Leyla Mollamahmutoğlu	109
Index	Subject and Author Index	113