Kistik Fibrozisin Prenatal Tanısı

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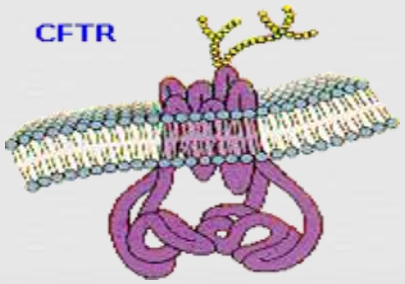
Kistik Fibrozis

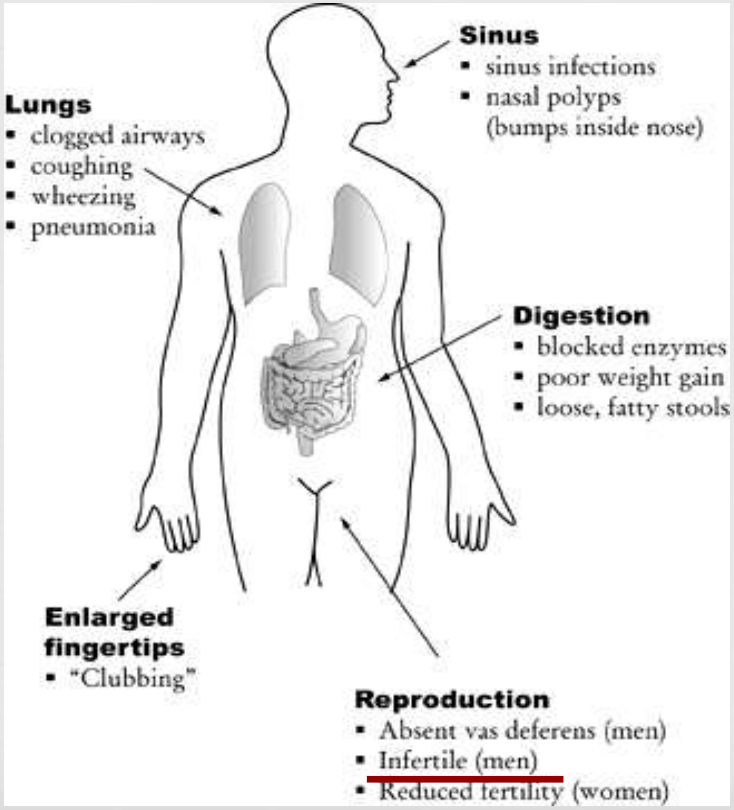
- Otozomal resesif geçiş gösteren genetik bir hastalık
- 7q kromozomdaki Fibrosis Transmembrane Conductance Regulator (CFTR) gen mutasyonu (~1700) sonucunda gelişmekte
- CFTR geni, epitelyal hücre membranındaki klor kanalından sodyum ve klorür iyonların geçişini kontrol eden bir süper protein sentezlemekte



Kistik Fibrozis

Mutasyon neticesinde ekzokrin organlardan anormal koyu kıvamlı mukus salgılanmakta;

- Respiratuar
- GİS, KC ve Pankreas
- Üreme sistemleri etkilenmekte



Kistik Fibrozis

En sık karşılaşılan ve tanınabilen 23 CFTR gen mutasyonu:

F508 del	del1507	R347P	R1162X
G542X	R553X	711+1G>T	2184delA
G551D	R117H	R560T	1898+1G>A
621+1G>T	3849+10kbC>T	3569delC	R334W
W1282X	1717–1G>T	A455E	3120+1G>T
N1303K	2789+5G>A	G85E	

Watson MS, Cutting GR, Desnick RJ, et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. Genet Med 2004;6:387–91.

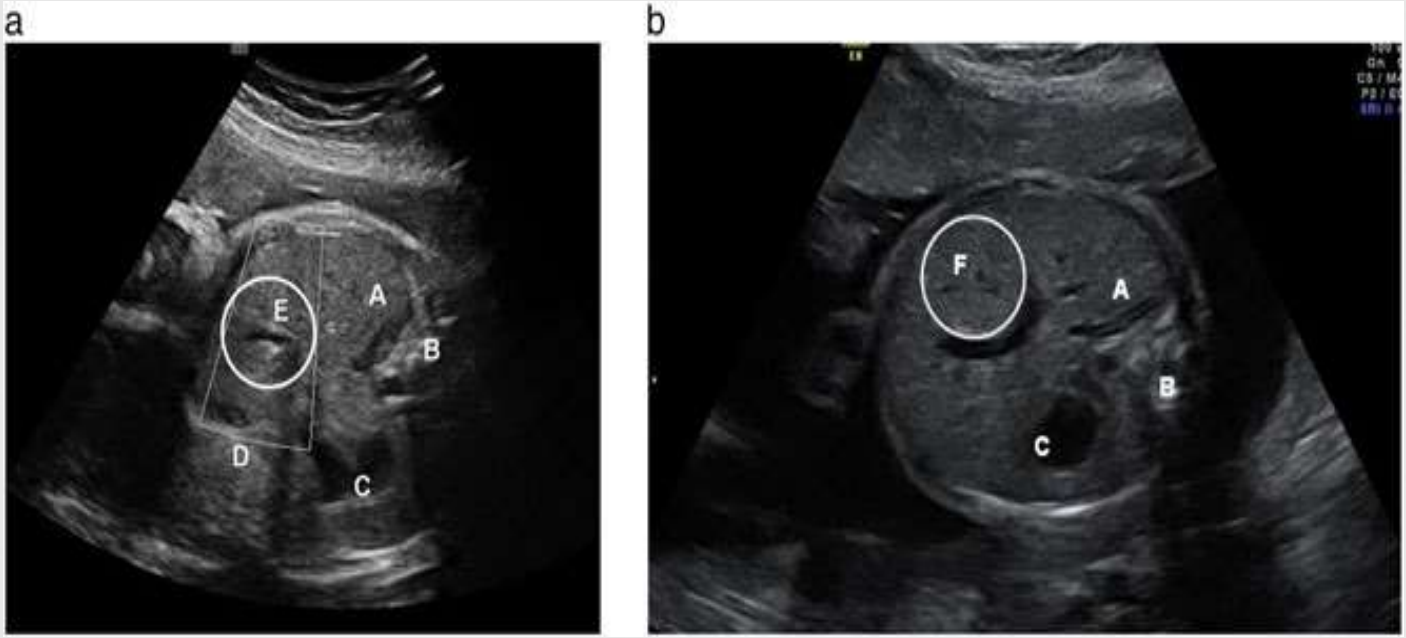
Epidemiyoloji

Etnik köken	KF insidansı	Taşıyıcı insidansı	Saptama oranı	Negatif test sonrası hesaplanmış taşıyıcılık oranı
Caucasian	1/3300	1/25	%80–88	1 / 166 (1/125–1/208)
Ashkenazi Jewish	1/3970	1/24	%94–97	1 / 600 (1/400–1/800)
Hispanic	1/8900	1/46	%57–72	1 / 135 (1/107–1/164)
African American	1/15 300	1/65	%65–69	1 / 198 (1/186–1/210)
Asian	1/35 000	1/94	%30–49	1 / 159 (1/134–1/184)

GR. Genetic epidemiology and genotype/phenotype correlations. NIH Consensus Development Conference on Genetic Testing for Cystic Fibrosis, 1997; ACOG Committee Opinion 325. Update on Carrier Screening for Cystic Fibrosis, 2005.

Ultrasonografik Bulgular

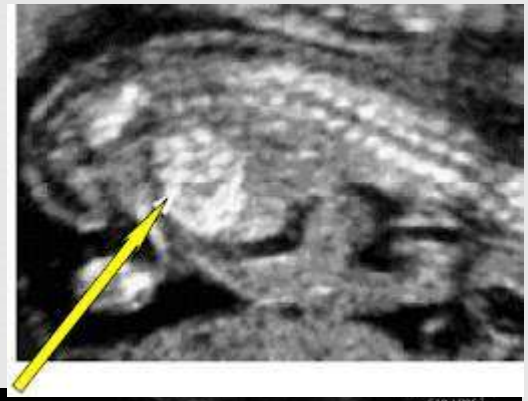
- Fetüste safra kesesinin izlenmemesi



A- adrenal gland; B- veretebral kolon; C- mide; D- umilikal ven; E-safra kesesi

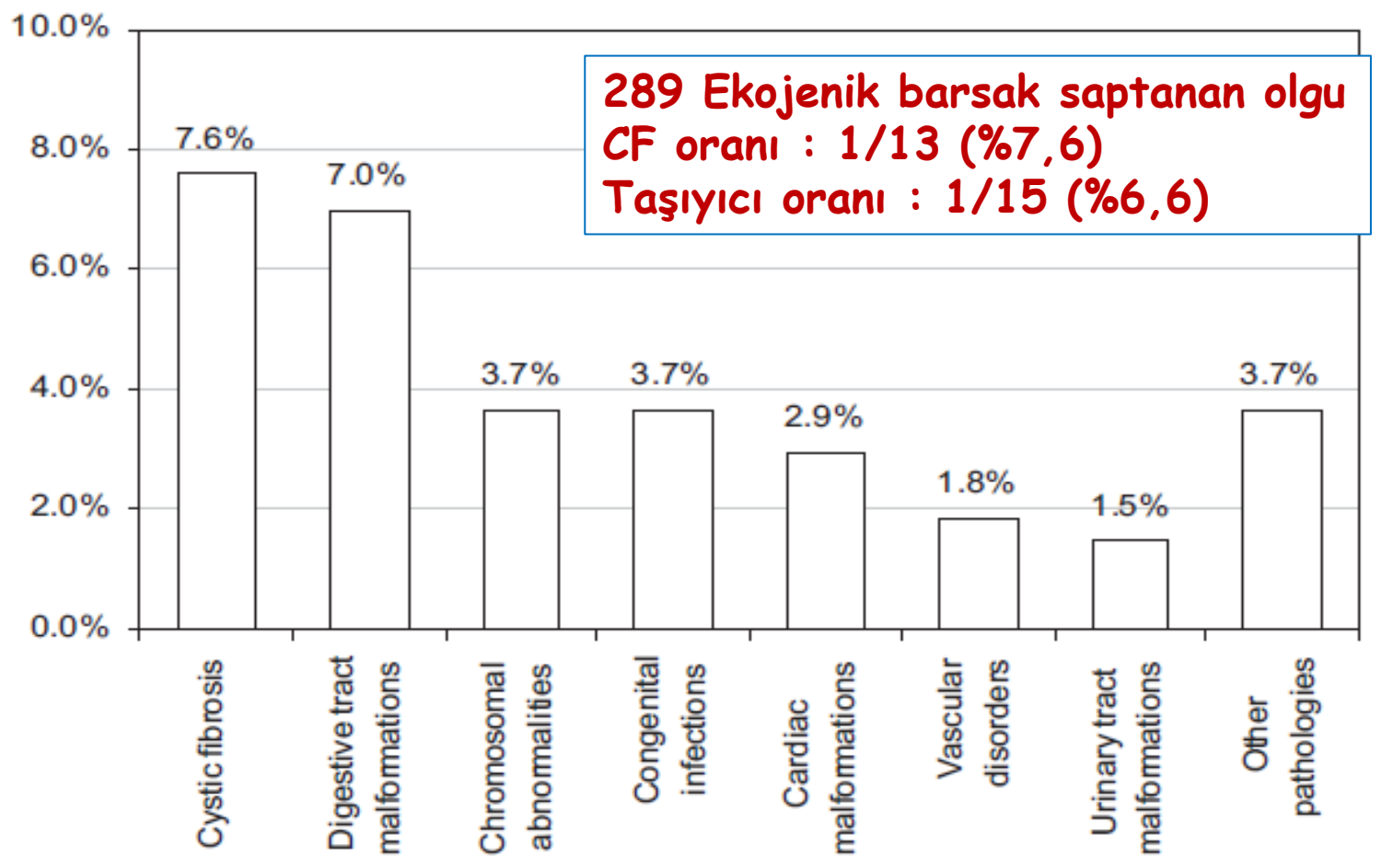
Ultrasonografik Bulgular

- Hiperekojen barsaklar: %0.1-1.8



Ultrasonografik Bulgular

Hiperekojen barsaklar



Scotet V, Duguépéroux I, Audrézet MP, et al. Focus on cystic fibrosis and other disorders evidenced in fetuses with sonographic finding of echogenic bowel: 16-year report from Brittany, France. Am J Obstet Gynecol 2010;203:592.e1-6.

Ultrasonografik Bulgular

Hiperekojen barsaklar

				Associated pathologies			
Study	y	Study duration	No. of FEB	CF	Chromosome abnormalities	Congenital infections	Digestive tract malformations
Present study	2010	16 y	289	7.6%	3.7%	3.7%	7.0%
Patel et al[26]	2004	7 y	109	1.8%	0.9%	—	—
Kesrouani et al[10]	2003	—	215	1.5%	7.0%	4.0%	3.0%
Simon-Bouy et al[11]	2003	2 y	682	3.1%	4.3%	2.8%	2.9%
Al Kouatly et al[9]	2001	8 y	175	3.6%	3.6%	0.9%	—
Ghose et al[7]	2000	2 y	60	5.0%	5.0%	0.0%	—
Strocker et al[8]	2000	5.5 y	131	0.0%	11.0%	9.9%	—
Berlin et al[4]	1999	3 y	244	0.8%	2.8%	—	—
Monaghan and Feldman[5]	1999	5 y	159	1.3%	4.0%	—	—
Yaron et al[6]	1999	6 y	79	2.5%	6.3%	6.3%	6.3%
Muller et al[3]	1998	5 y	209	3.3%	—	—	—

CF, cystic fibrosis; *FEB*, fetal echogenic bowel.

Scotet. Outcome of fetuses with echogenic bowel. Am J Obstet Gynecol 2010.

Scotet V, Duguépéroux I, Audrézet MP, et al. Focus on cystic fibrosis and other disorders evidenced in fetuses with sonographic finding of echogenic bowel: 16-year report from Brittany, France. Am J Obstet Gynecol 2010;203:592.e1-6.

Ultrasonografik Bulgular

- Hiperekojen barsak veya Megakolon:

  %3,1 (20/641)

- Hiperekojen barsak + Megakolon:

  %17 (5/29)

- Hiperekojen barsak + Safra kesesi görülmemesi:

  %25 (2/8)

F. Muller et al. Predicting the Risk of Cystic Fibrosis With Abnormal Ultrasound Signs of Fetal Bowel: Results of a French Molecular Collaborative Study Based on 641 Prospective Cases. American Journal of Medical Genetics 110:109–115 (2002)

Ultrasonografik Bulgular

- İzole hiperekojen barsak olanlarda:

  %3,9 (9/229)

- Safra kesesi görülemeyen fetüslerde:

  %13,5 (5/37)

- Hiperekojen barsak + Safra kesesi görülmemesi:

  %45,5 (5/11)

Sonuç: 45.5% vs 3.9%, **RR = 11.6**

Dugue´pe´roux I, Scotet V, Audrezet MP, Saliou A, Blayau M, Schmitt S, Kitzis A, Ferec C (2010) Nonvisualization of the gallbladder: a major risk of cystic fibrosis when associated with echogenic bowel.
European Cystic Fibrosis Conference, Valencia, pp S11

Ultrasonografik Bulgular

Ultrasonda anormal barsak bulgusu olan **694** olgunun **30**'u KF tanısı almış. (%4,3)

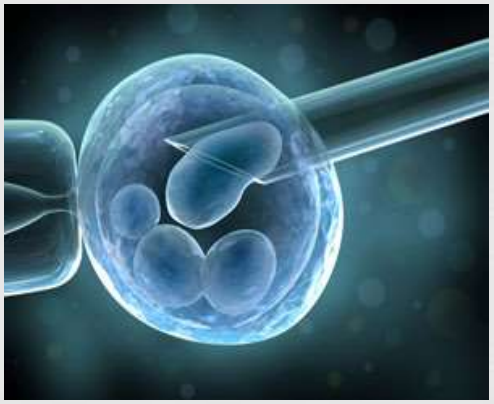
Ultrasound signs	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Likelihood ratio (LR) (95% CI)
Abdominal calcifications	0.0	96.8 (94.7–98.2)	0
Isolated non-visualization of gallbladder	0.0	98.7 (97.2–99.5)	0
Isolated hyperechogenic bowel	26.7 (14.2–44.4)	35.9 (31.7–40.4)	0.42 (0.23–0.76)
Ascites	3.3 (0.6–16.7)	97.2 (95.3–98.4)	1.19 (0.16–8.81)
Hyperechogenic bowel + ascites	0.0	96.6 (94.5–98.0)	0
Meconium peritonitis	6.7 (0.2–21.3)	96.6 (94.5–97.9)	1.94 (0.47–8.04)
Isolated loop dilatation	10.0 (3.5–25.6)	96.4 (94.7–98.0)	3.10 (0.95–10.1)
Hyperechogenic bowel + loop dilatation	23.3 (11.8–40.9)	91.2 (88.2–93.5)	2.65 (1.30–5.41)
Hyperechogenic bowel + non-visualization of the gallbladder	6.7 (0.2–21.3)	98.3 (96.6–99.1)	3.87 (0.86–17.45)
Hyperechogenic bowel + loop dilatation + non-visualization of the gallbladder	13.3 (0.05–29.7)	99.6 (98.4–99.9)	31.40 (5.91–162.51)

Duyarlılık: %0-26,7

Alix de Becdelie`vre et al. Comprehensive description of CFTR genotypes and ultrasound patterns in 694 cases of fetal bowel anomalies: a revised strategy. Hum Genet (2011) 129:387–396

Prenatal Tanı

- Koriyonik villüs örneklemesi
- Amniosentez
- Preimplantasyon genetik tanı (PGD)



Prenatal taramayı kimlere yapalım ?

The American College of Obstetricians and Gynecologists

Women's Health Care Physicians

COMMITTEE OPINION

Number 486 • April 2011 *(Replaces No. 325, December 2005)*

Committee on Genetics

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Update on Carrier Screening for Cystic Fibrosis

Prenatal tarama

- Çiftlerin KF'li çocukları varsa
- Anne KF taşıyıcıysa ve babanın genetik incelemesi yoksa veya babanın kimliği belli değilse
- Anne ve baba taşıyıcıysa
- Çiftlerde KF ve taşıyıcılık saptanmaması fakat soygeçmişlerinde KF vakasının olması
- Babanın KF hastası olması veya infertil/subfertil olması (vas deferens anomalisi)
- KF'in 2 mutasyonu olup KF hastalığın tanısını almayan çiftlere

Kistik Fibrosis

- Fetüste KF saptanırsa gebeliğin sonlandırılması önerilebilir. Ancak;

KF'li olgularda:

  - Zeka etkilenmez,
  - Ortalama hayat beklentisi 37 yıldır,
  - Ölüm genellikle akciğer hasarı nedeniyle olur,
  - Olguların %15'i hafif seyreder ve ortalama 56 yıl yaşar,

Faydalı linkler

- Cystic Fibrosis Foundation
  http://www.cff.org
  http://cysticfibrosis.com
- GeneTests and GeneReviews
  http://www.genetests.org
- National Society of Genetic Counselors
  http://www.nsgc.org
- Mountain States Genetics Network
  http://www.mostgene.org

Sabrınız için teşekkür ederim