17. BÖLÜM

NON-INVAZİV PRENATAL TARAMA TEKNOLOJİSİ VE GELECEĞİ

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GİRİŞ

Non-invazif prenatal tarama (NIPT), gebelik sırasında maternal kandan fetüse ait genetik anormallikleri belirlemeye yönelik yapılan bir testtir. NIPT, maternal plazma içinde dolaşan hücre içermeyen serbest fetal DNA'dan (circulating cell free fetal-ccffDNA) fetüse ait bir takım genetik anormallikleri öngörmeye yönelik bir testtir(1). Pek çok ülkede, trizomi 21 (Down sendromu), 18 (Edward sendromu) ve 13 (Patau sendromu) için tarama rutin doğum öncesi takiplerin bir parçası olarak sunulmaktadır. Bu, kombine tarama (ense kalınlığı, gebelikle ilişkili plazma protein A (PAPP-A), insan koryonik gonadotropin β (βHCG) ve anne yaşı) kullanılarak gebeliğin ilk tremesterinde veya dörtlü tarama (β HCG, konjuge olmayan östriol, α-fetoprotein ve inhibin A) kullanılarak ikinci tremesterde yapılmaktadır. Bu testlerde yüksek risk saptanan gebelere koryonik villus örneklemesi veya amniyosentez invaziv testlerinin yapılması önerilmektedir. Bu invaziv prosedürlerin düşüğe yol açma riski bulunmaktadır(2). NIPT bu riskleri ortadan kaldırmaya yönelik geliştirilmekte olan en yeni tarama aracı olarak güncel prosedürler arasında yerini almaya başlamıştır.

SİRKÜLE(SERBEST) FETAL DNA

Gebelikte, gelişmekte olan fetüse ait hücre dışı serbest DNA (cffDNA), erkek fetüs taşıyan gebelerin plazmasında Y kromozoma ait DNA'nın tespit edilmesi ile bulunmuştur(1) ccffDNA'nın kaynağı plasentanın sinsityotrofoblast tabakasıdır(3). Bir yıl sonra Lo ve ark., fetal DNA konsantrasyonunun maternal plaz-

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tespitini zorlaştıran homolog psödojenlere sahip genler, en önemlisi CYP21A2 ile ilişkili konjenital adrenal hiperplazide(95) RMD yaklaşımlarının aksine, RHD klinik olarak uygulanmaktadır ve Duchenne musküler distrofi(96), spinal musküler atrofi(97) ve kistik fibrozis(98) hastalıkları için NIPT hizmetleri artık Birleşik Krallık Sağlık Sisteminde mevcuttur.

Son zamanlarda, dPCR ve NGS gibi gelişmiş teknolojiler yüksek hassasiyetleri ve maternal plazma DNA'sından tüm fetal genomu açığa çıkarma olanakları nedeniyle NIPT'nin klinik uygulamasına izin vermişlerdir. Gelecekte, bu yöntemlerin anneden miras alınan mutasyonları da tespit edebilmesi beklenmektedir(99,100). cffDNA'da tüm fetal genom izlenebilmektedir ve genom sekanslama metodolojileri, ticari sağlayıcıların, cinsiyet kromozom anormallikleri, NOT'lar ve CNV sendromları dahil olmak üzere daha geniş bir fetal genetik anormallik yelpazesini rapor etmesine izin vermiştir. Yeni gelişen teknoloji ile NIPT ile babadan kalıtılanlar dahil olmak üzere monogenik hastalıkların tümüne yönelik ön tarama imkanının ailelere sunulması gelecek vizyonları içinde yerini almaya başlamıştır. Küçük CNV'lerin tespiti ve yorumlanmasının açıklığa kavuşması ile tüm genom sekanslama tabanlı NIPT yaklaşımının prenatal takiplerde hekim ve danışan arasındaki belirsizlikleri en aza indirmesi umulmaktadır.

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