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Knowledge and Attitude of Pregnant Women Undergoing Cell-free DNA Screening at the King Chulalongkorn Memorial Hospital

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ABSTRACT

Objectives: To investigate the knowledge and attitude of pregnant women before undergoing cell-free DNA screening at King Chulalongkorn Memorial Hospital (KCMH).

Materials and Methods: A cross-sectional study recruited 400 singleton pregnant women who underwent cell-free DNA screening at KCMH from December 2016 to August 2017. Self-administered questionnaires were used to evaluate participants' knowledge and attitude.

Results: Four-hundred pregnant women answered the questionnaires and 344 responses were considered valid. The maternal age ranged from 23 to 46 years and mean age was 34.8 ± 3.6 years. Almost all of the participants answered correctly about the test's ability to detect trisomy 21, trisomy 18, trisomy 13, and fetal sex (96.8, 83.7, 84.8, and 93.9% respectively). Eighty-nine percent of the women answered correctly about the time to start cell-free DNA testing, and 68% answered correctly about detection rate of trisomy 21. Some participants had misconceptions about the test's ability such as false negative rate, thalassemia screening, fetal malignancy detection, autistic detection, cleft lip-cleft palate detection, and the option of termination of pregnancy if the screening was positive. Seventy-nine percent were aware of the possibility of re-sampling. Additional data showed that participants had positive attitude towards cell-free DNA screening, and preferred to use it again for future pregnancy.

Conclusion: Our study showed that the majority of the participants had good knowledge of the test's ability to detect trisomy, and a possibility of re-sampling. However, almost half of the participants misunderstood that it could detect all genetic abnormalities. This study showed the magnitude of expectations and misunderstandings about cell-free DNA screening.

Keywords: cell-free DNA, NIPT, singleton, knowledge, attitude

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ความรู้และทัศนคติของหญิงตั้งครรภ์ที่เข้ารับการตรวจกรองโดยวิธีเซลล์ฟรีดีเอ็นเอในโรงพยาบาลจุฬาลงกรณ์

พัชราภรณ์ ชโลปกรณ์, ศักนัน มะโนทัย

บทคัดย่อ

วัตถุประสงค์: *เพื่อประเมินความรู้และทัศนคติของหญิงตั้งครรภ์ก่อนเข้ารับการตรวจคัดกรองเซลล์ฟรีดีเอ็นเอที่โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย*

วัสดุและวิธีการ: *เป็นการศึกษาภาคตัดขวาง โดยเลือกกลุ่มตัวอย่างจากหญิงตั้งครรภ์เดี่ยวจำนวน 400 คน ที่จะเข้ารับการตรวจคัดกรองเซลล์ฟรีดีเอ็นเอในโรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย ในช่วงเดือนธันวาคม พ.ศ.2559 ถึงเดือนสิงหาคม พ.ศ.2560 โดยใช้แบบสอบถามในการประเมินความรู้และทัศนคติของหญิงตั้งครรภ์ก่อนได้รับคำปรึกษาทางพันธุกรรม*

ผลการศึกษา: *หญิงตั้งครรภ์ 400 คน ตอบแบบสอบถาม โดยมีผู้ตอบแบบสอบถามครบถ้วนจำนวน 344 คน อายุอยู่ระหว่าง 23 ถึง 46 ปี โดยมีอายุเฉลี่ย 34.8 ± 3.6 ปี ผู้เข้าร่วมงานวิจัยเกือบทั้งหมดตอบถูกเกี่ยวกับความสามารถในการตรวจหา trisomy 21, trisomy 18, trisomy 13 และเพศของทารก (ร้อยละ 96.8, 83.7, 84.8 และ 93.8 ตามลำดับ) ร้อยละ 89 ของผู้เข้าร่วมวิจัย ตอบถูกเกี่ยวกับเวลาในการเริ่มการตรวจเซลล์ฟรีดีเอ็นเอ และร้อยละ 68 ตอบถูกเกี่ยวกับอัตราการตรวจหา trisomy 21 ผู้เข้าร่วมงานวิจัยส่วนหนึ่งยังมีความเข้าใจผิดเกี่ยวกับการทดสอบ เช่น อัตราการเกิดผลลบลวง, การตรวจคัดกรองธาลัสซีเมีย, การตรวจพบมะเร็งในทารก, การตรวจพบออทิสติก, การตรวจพบปากแหว่งเพดานโหว่ และการตัดสินใจยุติการตั้งครรภ์ หากผลการคัดกรองเป็นบวก ร้อยละ 79 ทราบว่าอาจมีโอกาสที่ต้องเจาะเลือดซ้ำ ในด้านทัศนคติต่อการตรวจเซลล์ฟรีดีเอ็นเอ ผู้เข้าร่วมงานวิจัยมีความพึงพอใจสูงต่อการทดสอบนี้ และมีแนวโน้มที่จะเลือกใช้ตรวจคัดกรองในครรภ์ถัดไป*

สรุป: *หญิงตั้งครรภ์ส่วนใหญ่มีความรู้เกี่ยวกับความสามารถของการทดสอบในด้านการตรวจหา trisomy และเข้าใจว่ามีโอกาสที่จะต้องถูกเก็บตัวอย่างเลือดซ้ำ อย่างไรก็ตามเกือบครึ่งหนึ่งของผู้เข้าร่วมงานวิจัยยังเข้าใจผิดว่าการทดสอบนี้สามารถตรวจพบความผิดปกติทางพันธุกรรมทั้งหมดได้ซึ่งแสดงให้เห็นว่า ผู้เข้าร่วมงานวิจัยมีความคาดหวังที่เกินจริง และยังมีความเข้าใจผิดเกี่ยวกับการตรวจคัดกรองเซลล์ฟรีดีเอ็นเอ การศึกษานี้สะท้อนให้เห็นถึงความสำคัญของการให้ความรู้ที่ถูกต้องในด้านความสามารถของการตรวจคัดกรองนี้ เพื่อให้เกิดความเข้าใจที่ถูกต้องต่อไป*

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Introduction

Nowadays, fetal chromosome abnormalities are seen as a major global problem. The most common chromosome disorder of live birth infants is Down syndrome. The prevalence increases as the maternal age increases[1,2]. A reference from CDC from 1979 to 2003 showed that the prevalence of Down syndrome increased up to 30% in the United States from 9.0 to 11.8 per 100,000 live births[3]. The prevalence of Down syndrome in Thailand also increased from 1 in 800 to 1 in 526[4]. This problem is considered to be significant because it affects the family and the society. Children with Down syndrome have delayed physical development and mental retardation. The Study of Health Intervention and Technology Assessment Program (HITAP) in 2011 estimated the lifelong cost of Down syndrome to be around 2,500,000 baht per person of which 40% are related to medical issues[5].

Prenatal screening technology was developed to detect genetic disorders. The conventional screenings consist of maternal age older than 35 years, ultrasound and biochemical markers in maternal serum. The detection rate varies between 30% to 94%. False positive rate is 5-10% and positive predictive value (PPV) is only 1-3%. Therefore, more than 95% of pregnant women would undergo unnecessary invasive prenatal diagnosis such as amniocentesis, and chorionic villi sampling which can result in procedure related complications. Important complications such as chorioamnionitis (0.1%), amniotic fluid leakage (2%), and miscarriage (0.5-1%) may occur when such invasive procedures are performed[6]. However, in 1997, circulating fetal cell-free DNA discovered by Dennis Lo was developed to be a noninvasive screening procedure. This technique was based on the knowledge that maternal serum contains fragments of DNA, a small proportion of which derives from placental cell apoptosis. In 2011, this new prenatal screening technology is called cell-free DNA noninvasive prenatal testing (NIPT)[7-9].

Cell-free DNA screening can be performed at as early as the 10th week of gestation. The detection rate of Down syndrome is 99%, false positive rate is less than 1% and PPV is 70-90%[10]. It is obvious that cell-free DNA screening can reduce the need for invasive procedure which is associated with miscarriage and infection risks[11]. Moreover, this test can be used to screen fetal trisomy 18, trisomy 13, other chromosomal aneuploidies, monosomy X and other sex chromosomal aneuploidies. The American College of Obstetricians and Gynecologists (ACOG) in 2015 recommended that pregnant women may choose cell- free DNA for screening regardless of their aneuploidy risks[12]. However, they should understand the limitations of this test to avoid over expectation because it does not truly provide absolute diagnosis. A positive result must undergo diagnostic test to confirm fetal genetic disorder.

Previous studies have shown that there was a difference in the knowledge and attitude towards cell-free DNA screenings. In Hong Kong, 70-90% of the pregnant women who tested positive by another aneuploidy screening had high knowledge about cell-free DNA screening's efficacy and limitations with positive attitude towards the test[13,14]. In contrast, only 30% of Japanese pregnant women knew the sensitivity and weakness of this test[15].

In Thailand, NIPT became available in July 2012 which attracted a lot of attention[16]. However there are no studies or data available regarding the knowledge and attitude towards cell-free DNA screening in Thailand. Our study investigated the knowledge and attitude of pregnant women undergoing cell-free DNA screening at the King Chulalongkorn Memorial Hospital (KCMH).

Materials and Methods

Study design and participants

This cross-sectional study recruited 400 pregnant women who were about to undergo cell-free DNA at the Division of Maternal-Fetal Medicine (MFM), King Chulalongkorn Memorial Hospital. Sample size was calculated from proportion of cell-free DNA knowledge at 0.7[13] and number of required participants was 323. We estimated that incomplete questionnaire responses would be approximately 20%. Singleton pregnant women who were more than 18 years old and had

gestational age of more than 10 weeks were enrolled into the study. Pregnant women with a multifetal pregnancy or who were illiterate were excluded from the study. The primary objective was to evaluate the knowledge of cell-free DNA screening in pregnant women undergoing this test at the KCMH. The secondary objective was to evaluate their attitude towards the test.

Data collection and tools

The questionnaire was developed by by one of the authors in Thailand validated by 3 maternal-fetal medicine specialists. The reliability of the test was calculated by Cronbach's Alpha. The questionnaire was administered to pregnant women who requested cell-free DNA screening prior to the routine pretest counseling. A rapid response questionnaire consisted of 5 pages, and was separated into 3 sections which were designed to assess demographic data, knowledge and attitude on cell-free DNA screening. The demographic section collected the following information: age, race, religion, education, career, address, underlying diseases, obstetric history and problems in previous pregnancies. The knowledge part assessed the participants' understanding of the test's ability, its detection rate, its limitations, concept of the screening test, and source of information on cell-free DNA screening. This part consisted of fill-in-the-blank questions and true-false questions. The attitude part asked the participants why they chose to do cell-free DNA screening, what they would do if the test yielded positive result and their satisfaction of doing the cell-free DNA screening. The attitudes toward having an abnormal test result were scored using a five-point Likert scale ranging from 1 to 5; 5 being the most concerned to 1 being unconcerned. Also, the satisfaction towards cell-free DNA screening test at the KCMH was scored using a five-point Likert scale ranging from 1 to 5; 5 being very satisfied to 1 being very dissatisfied. A score of 4 or more indicated that the participant had a positive attitude towards cell-free DNA screening. The participants completed the questionnaire before pretest counseling.

Statistics analysis

Data were statistically analyzed using SPSS for Windows version 22. Descriptive statistics were used to calculate proportions. The differences between two groups were calculated by Chi-square tests or Fisher's Exact test where appropriate. The statistical significance was set at p-value of less than 0.05.

Ethical considerations

The study protocol and the questionnaires were approved by the Research Ethics Committee, Faculty of Medicine, Chulalongkorn University. Written informed consent was obtained from all women prior to recruiting them into the study.

Results

1. Demographic data:

Four-hundred pregnant women who underwent cell-free DNA screening at the KCMH from December 2016 to August 2017 answered the questionnaires. The reliability of the test by Cronbach's Alpha was 0.702. From 400 responses, 344 were considered valid. Fourteen percent (56/400) of the questionnaires were considered to be incomplete, and were excluded from the analysis. All participants were Thai. Most of the participants lived in the central part of Thailand. Seventy-four percent (256/344) lived in Bangkok. The demographic data are summarized in Table 1. The maternal age ranged from 23 to 46 years and the mean age was 34.8±3.6 years. Ninety-six percent of the participants had bachelor degree or higher education level. The obstetric history showed that 50.6% of the participants were primigravida most of whom were younger than 35 years old. Two women (0.6%) out of 344 participants had an abnormal child in a previous pregnancy; one child had Down syndrome and the other child had undescended testis. One point seven percent of the participants had an individual with Down syndrome in their families. Two percent had another prenatal screening before this present study; four women had a first trimester screening, one woman had a triple screen test and two women had a quadruple screen test.

Table 1. Demographic data of the participants undergoing cell-free DNA screening.

Demographic data	Total (%) N = 344	Age < 35 y (%) N = 149	Age ≥ 35 y (%) N = 195
Age (mean ± SD)	34.82 ± 3.581	31.61 ± 2.503	37.28 ± 1.978
BMI (mean ± SD)	22.11 ± 3.232	21.54 ± 3.161	22.54 ± 3.227
Race			
Thai	344 (100)	149 (100)	195 (100)
Region			
Central	310 (90.1)	140 (94.0)	170 (87.2)
North	6 (1.7)	0 (0)	6 (3.1)
South	3 (0.9)	2 (1.3)	1 (0.5)
East	17 (4.9)	6 (4.0)	11 (5.6)
West	1 (0.3)	0 (0)	1 (0.5)
Northeastern	7 (2.0)	1 (0.7)	6 (3.1)
Religion			
Buddhism	334 (97.1)	149 (100)	185 (94.9)
Christianity	3 (0.9)	0 (0)	3 (1.5)
Islam	5 (1.5)	0 (0)	5 (2.6)
Others	2 (0.6)	0 (0)	2 (1.0)
Education			
< Bachelor	13 (3.8)	6 (4.0)	7 (3.6)
Bachelor	234 (68.0)	104 (69.8)	130 (66.7)
> Bachelor	97 (28.2)	39 (26.2)	58 (29.7)
Career			
Government	57 (16.6)	26 (17.4)	31 (15.9)
Officer	144 (41.9)	70 (47.0)	74 (37.9)
Employee	3 (0.9)	0 (0)	3 (1.5)
No occupation	20 (5.8)	8 (5.4)	12 (6.2)
Business	59 (17.2)	28 (18.8)	31 (15.9)
Others	61 (17.7)	17 (11.4)	44 (22.6)
Gravida			
1	174 (50.6)	91 (61.1)	83 (42.6)
>1	170 (49.4)	58 (38.9)	112 (57.4)
Abortion			
No	274 (79.7)	124 (83.2)	150 (76.9)
Yes	70 (20.3)	25 (16.8)	45 (23.1)
Abnormal Children			
No	342 (99.4)	148 (99.3)	194 (99.5)
Yes	2 (0.6)	1 (0.7)	1 (0.5)
Medical Complication			
No	340 (98.8)	149 (100)	191 (97.9)
Yes	4 (1.2)	0 (0)	4 (2.1)

2. Knowledge about cell-free DNA screening

This study showed that pregnant women who underwent cell-free DNA screening at the KCMH knew about the test's ability to screen for trisomy 13 (84.9%), trisomy 18 (83.7%), trisomy 21 (96.8%), and fetal sex chromosome (93.9%). The majority of the participants knew that it was necessary to continue testing with an invasive diagnosis procedure (79.9%) if the screening result was positive and also, 79.1% percent of the women were aware that there was a chance of re-sampling for screening. The majority of the participants answered correctly about the sensitivity of the test and the earliest time to perform the test. However, less than 30% of the participants knew that the currently available test could not be used to screen for all chromosome disorders and other fetal anomalies such as thalassemia, autism, cleft lip and cleft palate. Only a minority knew that the test had a chance of false positive and false negative results. One-fourth (25%) misunderstood that after a positive cell-free DNA screening result, there was no need for confirmation test before terminating the pregnancy. Most of the participants obtained information about cell-free DNA screening from the internet, their primary doctors and friends. Data regarding the participants' knowledge are summarized in Tables 2 and 3.

Table 2. Knowledge of cell-free DNA screening in pregnant women undergoing cell-free DNA.

Correct answer of cell-free DNA test's ability	Total (%) N = 344	Age < 35 y (%) N = 149	Age ≥ 35 y (%) N = 195	p value
Down syndrome	333 (96.8)	142 (95.3)	191 (97.9)	0.167
Trisomy 13	292 (84.9)	137 (91.9)	155 (79.5)	0.001
Trisomy 18	288 (83.7)	132 (88.6)	156 (80.0)	0.032
Sex	323 (93.9)	141 (94.6)	182 (93.3)	0.618
All chromosome disorders	55 (16.0)	28 (18.8)	27 (13.8)	0.215
Blood group	68 (19.8)	33 (22.1)	35 (17.9)	0.333
Thalassemia	64 (18.6)	30 (20.1)	34 (17.4)	0.524
Cancer	113 (32.8)	56 (37.6)	57 (29.2)	0.102
Autistic child	73 (21.2)	47 (31.5)	26 (13.3)	< 0.0001
Cleft lip and cleft palate	97 (28.2)	48 (32.2)	49 (25.1)	0.148

Table 3. Knowledge of cell-free DNA test's abilities in pregnant women undergoing cell-free DNA.

Cell-free DNA	Total (%) N = 344
can be performed at as early as on the 10th week of gestation	306 (89.0)
has a sensitivity around 99%	233 (67.7)
there is a chance to have false positive (< 1%)	170 (49.4)
there is a chance to have false negative	92 (26.7)
is a screening test and need to have invasive diagnostic test	275 (79.9)
cannot terminate pregnancy if the result of the cell-free DNA is positive	258(75.0)
may need resampling	272 (79.1)

3. Attitudes toward cell-free DNA screening

Fig. 1. shows that the top three personal reasons to undergo cell-free DNA screening test were advanced maternal age, concern of complications of invasive diagnostic test, and concern of pain from the invasive test. Fifty-five point two percent of the participants were "most concerned" (had a score of 5) and 40.1% were "concerned" (had a score of 4) about receiving a positive result from the cell-free DNA screening. Seventy-six percent of the participants would decide to perform further invasive diagnosis test (i.e., amniocentesis) if the result of the cell-free DNA screening test was positive. Seventy-seven point six percent of the participants would terminate the pregnancy if the fetus was confirmed with Down syndrome (Fig. 2). Thirty-eight point seven percent of the participants were very satisfied (had a score of 5) and 53.2% of the participants were satisfied (had a score of 4) to have cell-free DNA screening (Fig. 3). Overall, most of the participants had a positive attitude towards cell-free DNA screening in the current and later pregnancies.

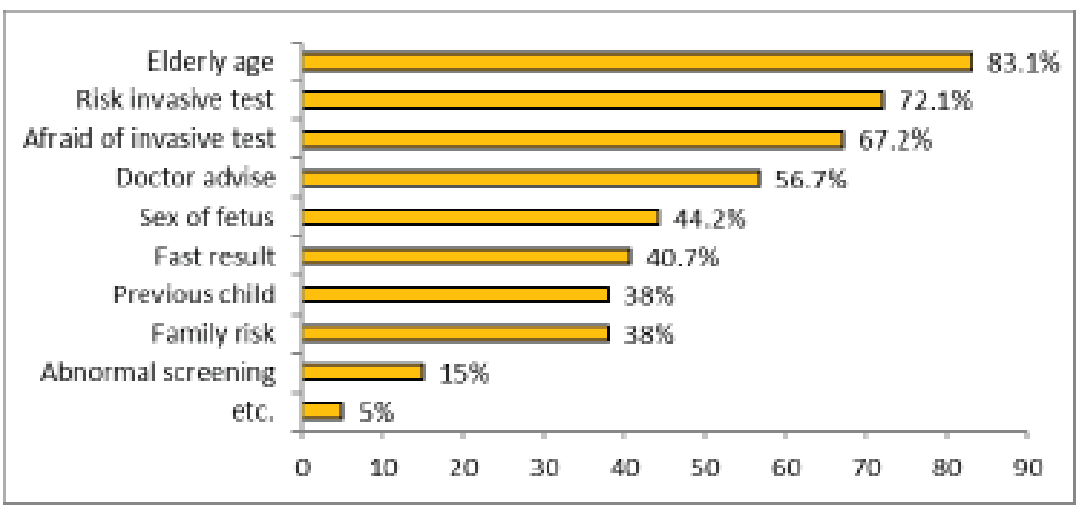

Fig. 1. Reasons to have cell-free DNA screening at the KCMH.

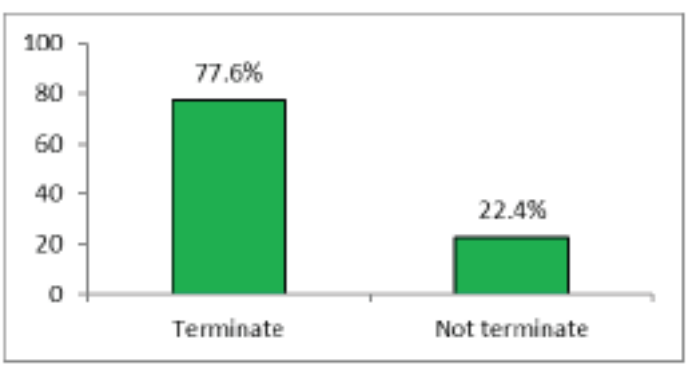

Fig. 2. Attitude towards positive prenatal diagnosis of Down syndrome to terminate pregnancy.

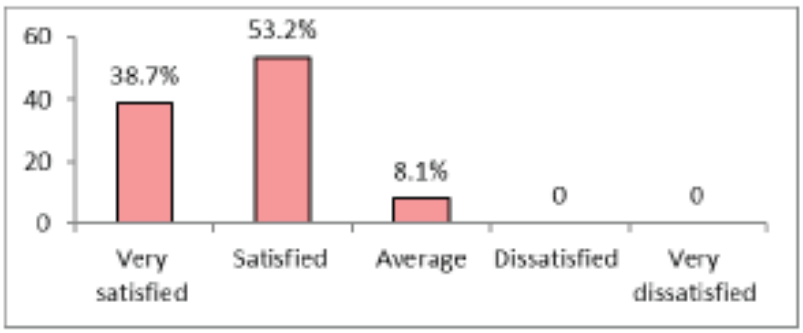

Fig. 3. Participants' satisfaction level of the cell- free DNA screening test at the KCMH.

Discussion

ACOG currently recommends offering cell-free DNA screening to high risk pregnant women, but also suggests that any woman may choose cell-free DNA screening. In this study, 43.31% of the participants undergoing cell-free DNA screening were in the low-risk group (age less than 35 years). This shows that cell-free DNA screening is widely accepted in low-risk women in Thailand.

A previous study from Japan which was conducted in 2015 reported that 75% of the participants knew that cell-free DNA screening can be used for screening Down syndrome but they did not know the test's ability to screen for trisomy 13 and trisomy 18[15]. For this study, more than 80% knew that the test can screen for trisomy 13, trisomy 18, trisomy 21 and fetal sex chromosome. This is likely due to the difference in population group between pregnant women in Japan and Thai pregnant women who sought cell-free DNA screening at KCMH.

The participants in this study had good knowledge of the test's detection rate which is similar to the study conducted in Hong Kong in 2015[13]. However, less than half of the participants in this study knew that the test could yield false positive and false negative results. Moreover, many of the participants at the KCMH seemed to have over expectation about the test's ability to screen for all chromosomal and other fetal abnormalities such as thalassemia, autism and so on. Previous studies showed that the knowledge of cell-free DNA screening of the pregnant women were based on the following factors: age, educational level, and interest in cell-free DNA screening[13-15,17]. In this study, we found that women in the younger age group had a better knowledge than the older age group about the test's ability to screen for trisomy 13 and trisomy 18.

This study is the first of its kind to assess the knowledge and attitude of pregnant women undergoing cell-free DNA screening in Thailand. There are several limitations in this study. Firstly, it is a descriptive study which was performed at a single center (KCMH). Thus, it may not represent the entire Thai population. Secondly, this study did not have the primary aim for subgroup comparison, so the result of subgroup analysis must be interpreted carefully.

Additional studies are needed to analyze the factors that affect the knowledge and attitudes in a study with a larger sample size.

Conclusion

In conclusion, our participants had good knowledge about the test's ability and had positive attitude towards cell-free DNA screening. However, there were some over expectation[18-20]. Additional study should provide the right information at the pretest counseling and evaluate whether it can improve the education and expectations in pregnant women undergoing cell-free DNA or not.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Wilson RD, Langlois S, Johnson JA. Mid-trimester amniocentesis fetal loss rate. J Obstet Gynaecol Can 2007;29:586-90.
2. Pariente G, Hasan L, Gadot Y, De Souza LR, Lebovic G, Berger H. Canadian women's attitudes toward noninvasive prenatal testing of fetal DNA in maternal plasma . J Matern Fetal Neonatal Med 2016;29:4008-14.
3. Centers for Disease Control and Prevention. Birth defects [Internet]. 2017 [cited 2016 Dec 19]. Available from:https://www.cdc.gov/ncbddd/birthdefects/downsyndrome/data.html.
4. Pangkanon S, Sawasdivorn S, Kuptanon C, Chotigeat U, Vandepitte W. Establishing of national birth defects registry in Thailand. J Med Assoc Thai 2014;97 Suppl 6:S182-8.
5. Pattanapesat J, Tanmookayakul U, Teerawattananon Y. Cost-benefit analysis of prenatal screening and diagnosis for Down syndrome in Thailand. J Health Sci 2012;21:667-84.
6. Wapner RJ. Prenatal diagnosis of congenital disorders. In: Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, Greene MF, editors. Creasy and Resnik's maternal-fetal medicine. 7th ed. Philadelphia: Elsevier 2014;417-64.
7. Lo YM, Corbetta N, Chamberlain PF, Rai V, Sargent IL, Redman CW, et al. Presence of fetal DNA in maternal plasma and serum. Lancet 1997;350:485-7.
8. Benn P, Cuckle H, Pergament E. Non-invasive prenatal testing for aneuploidy: current status and future prospects. Ultrasound Obstet Gynecol 2013;42:15-33.
9. Benn P. Non-invasive prenatal testing using cell free DNA in maternal plasma: Recent developments and future prospects. J Clin Med 2014;3:537-65.
10. Gil MM, Accurti V, Santacruz B, Plana MN, Nicolaides KH. Analysis of cell-free DNA in maternal blood in screening for aneuploidies: updated meta-analysis. Ultrasound Obstet Gynecol 2017;50:302-14.
11. Taglauer ES, Wilkins-Haug L, Bianchi DW. Review: cell-free fetal DNA in the maternal circulation as an indication of placental health and disease. Placenta 2014;35 Suppl:S64-8.
12. Committee Opinion. No. 640: Cell-free DNA screening for fetal aneuploidy. Obstet Gynecol 2015;126:e31-7.
13. Kou KO, Poon CF, Tse WC, Mak SL, Leung KY. Knowledge and future preference of Chinese women in a major public hospital in Hong Kong after undergoing non-invasive prenatal testing for positive aneuploidy screening: a questionnaire survey. BMC Pregnancy Childbirth 2015;15:199.
14. Choi SSN, Cahn LW, WWK T. Pregnant Women's attitudes to and knowledge of non-invasive prenatal testing in Down syndrome screening in Hong Kong. Hong Kong J Gynaecol Obstet Midwifery 2014;14:43-50.
15. Mikamo S, Nakatsuka M. Knowledge and Attitudes toward Non-invasive Prenatal Testing among Pregnant Japanese Women. Acta Med Okayama 2015;69:155-63.
16. Manotaya S, Xu H, Uerpairojkit B, Chen F, Charoenvidhya D, Liu H, et al. Clinical experience from Thailand: noninvasive prenatal testing as screening tests for trisomies 21, 18 and 13 in 4736 pregnancies. Prenat Diagn 2016;36:224-31.
17. Farrell R, Hawkins A, Barragan D, Hudgins L, Taylor J. Knowledge, understanding, and uptake of noninvasive prenatal testing among Latina women. Prenat Diagn 2015;35:748-53.
18. Sahlin E, Nordenskjold M, Gustavsson P, Wincent J, Georgsson S, Iwarsson E. Positive attitudes towards Non-Invasive Prenatal Testing (NIPT) in a Swedish cohort of 1,003 pregnant women. PLoS One 2016;11:e0156088.
19. Allyse M, Sayres LC, Goodspeed TA, Cho MK. Attitudes towards non-invasive prenatal testing for aneuploidy among US adults of reproductive age. J Perinatol 2014;34:429-34.
20. Verweij EJ, Oepkes D, de Boer MA. Changing attitudes towards termination of pregnancy for trisomy 21 with non-invasive prenatal trisomy testing: a population-based study in Dutch pregnant women. Prenat Diagn 2013;33:397-9.