Journal of Human Genetics (2016) 61, 879–884

www.nature.com/jhg

ORIGINAL ARTICLE

Nationwide survey for current clinical status of amniocentesis and maternal serum marker test in Japan

Hidehiko Miyake[1], Shigehito Yamada[1], Yosuke Fujii[2], Hideaki Sawai[3], Naoko Arimori[4], Yasuko Yamanouchi[5], Yuka Ozasa[6], Makoto Kanai[7], Haruhiko Sago[8], Akihiko Sekizawa[9], Fumio Takada[10], Hideaki Masuzaki[11], Yoichi Matsubara[12], Fumiki Hirahara[13] and Koji Kugu[14]

Prenatal testing has been provided in Japan over the past several decades. However, it is difficult to assess the clinical status of amniocentesis (AC) and maternal serum markers (MSM) because obstetricians can perform these tests without registration. This study aims to investigate the current clinical status of AC and MSM in Japan. We conducted a questionnaire study that was intended for a total of 5622 Japanese obstetrics/gynecology facilities during October 2013 to January 2014. The response rate was 40.8% (2295/5622). Of the 2295 facilities, 864 performed MSM (37.7%), 619 performed AC (27.0%) and 412 performed both (18.0%). The average number of MSM tests was 2.0 per month (range 0–52), and the average number of AC tests was 2.4 per month (range 0–30). Involvement of genetic professionals, such as clinical geneticists (CGs) and certified genetic counselors (CGCs), contribute to a content-rich explanation and management of difficult issues and lengthened the explanation time. Nevertheless, relatively few facilities employed these specialists (MSM: 96/864 and AC: 128/619). This is the first study to highlight the current clinical status of AC and MSM tests in Japan. Active involvement of CGs and CGCs can provide more appropriate genetic counseling for prenatal tests.
Journal of Human Genetics (2016) **61,** 879–884; doi:10.1038/jhg.2016.67; published online 30 June 2016

INTRODUCTION

Prenatal testing has been provided in Japan over the past several decades, but the regulations for prenatal diagnosis are based on guidelines, not legislation. The Japan Society of Obstetrics and Gynecology has recommended that prenatal testing should not be routinely offered but should be available on an individual basis if requested.[1] However, there are differences in the regulation of prenatal tests conducted by different methods. For conducting preimplantation genetic testing and cell-free fetal DNA genetic testing in maternal plasma (noninvasive prenatal testing), accreditation of medical facilities by academic societies is required. Moreover, case registration for such tests is compulsory. In contrast, obstetricians can perform other 'conventional' prenatal tests, such as amniocentesis (AC) and maternal serum marker (MSM) tests, without accreditation and case registration.

In the present system, it has been difficult to assess the use of 'conventional' AC and MSM prenatal testing. This situation is inconvenient from the point of view of governance of prenatal testing. Previously, some research has been performed to investigate the status of conventional prenatal diagnosis and screening in Japan. In 1997, Matsuda and Suzumori[2] conducted a questionnaire study of medical facilities, representing ~80% of the facilities providing prenatal diagnosis, including AC and chorionic villi sampling. Sasaki *et al.*[3] surveyed nationwide clinical laboratories to cover most cases of genetic prenatal tests performed in Japan from 1998 to 2008. Nishiyama *et al.*[4] reported the status of AC testing; however, their research was based on the data from a prenatal testing laboratory. Therefore, the clinical environment of prenatal testing has remained obscure for the entire of Japan.

In 2014, the total number of births in Japan was 1 003 539. Of those, 99.1% occurred in medical facilities, with the numbers of births at hospitals and clinics being 536 279 and 458 250, respectively.[5] These facts may reflect the traditional Japanese childbirth conditions that feature a large number and a diverse range of

[1]Clinical Genetics Unit, Kyoto University Hospital, Kyoto, Japan; [2]Unit of Statistical Genetics, Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan; [3]Department of Obstetrics and Gynecology, Hyogo College of Medicine, Nishinomiya, Japan; [4]The School of Health Sciences, Niigata University, Niigata, Japan; [5]Department of Social Work, Faculty of Health and Welfare, Kawasaki University of Medical Welfare, Kurashiki, Japan; [6]Department of Nursing, Tokyo Medical and Dental University Medical Hospital, Tokyo, Japan; [7]Department of Family and Child Nursing, and Midwifery, Shinshu University School of Health Sciences, Matsumoto, Japan; [8]Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development, Tokyo, Japan; [9]Department of Obstetrics and Gynecology, School of Medicine, Showa University, Tokyo, Japan; [10]Department of Medical Genetics and Genomics, Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan; [11]Department of Obstetrics and Gynecology, Nagasaki University, Nagasaki, Japan; [12]National Research Institute for Child Health and Development, Tokyo, Japan; [13]National Hospital Organization Yokohama Medical Center, Yokohama, Japan and [14]Department of Obstetrics and Gynecology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan
Correspondence: Dr H Miyake, Clinical Genetics Unit, Kyoto University Hospital, 54 Shogoin-Kawaharacho, Sakyo-ku, Kyoto 606-8507, Japan.
E-mail: hidehiko@pluto.dti.ne.jp
Received 9 March 2016; revised 18 April 2016; accepted 10 May 2016; published online 30 June 2016

small-scale birthing facilities providing medical treatments at the patient's own expense.[6] Based on this situation, it is considered that almost all obstetric/gynecological facilities have opportunities to consult pregnant women on prenatal diagnosis.

Appropriate prenatal screening and diagnostic testing options are typically presented to patients in the context of a prenatal genetic counseling session.[1,7,8] The Japanese qualifications for genetic health-care professionals include clinical geneticists (CGs with an MD) and certified genetic counselors (CGCs who were non-MD). In 2015, there were 1276 CGs and 182 CGCs. However, the Japanese medical specialty education system does not regard clinical genetics as a basic specialty. Moreover, the number of medical facilities with obstetrics departments was 1361 in 2014, that is, 14 less than that in 2013.[9] Thus, not all of the clinical genetic professionals might be involved in prenatal testing.

Noninvasive prenatal testing started in April 2013 in Japan. Before start of the testing, newspaper reports about noninvasive prenatal testing in August 2012 had aroused social interest on prenatal diagnosis.[10] However, clinical status of prenatal genetic counseling on Japanese facilities was unknown. On the basis of these circumstances, we conducted a nationwide study among obstetricians and gynecologists regarding prenatal testing, particularly AC and MSM, in Japan. Moreover, we evaluated the involvement of genetic professionals in prenatal testing.

MATERIALS AND METHODS

We conducted a nationwide survey based on the total membership in the Japan Association of Obstetricians and Gynecologists. A total of 5622 facilities were initially included in this survey. We choose an anonymous, self-administered questionnaire as a study format. The questionnaire was mailed to the person in charge of an obstetrics/gynecology department at each facility in October 2013. Via post, we received the questionnaire between October 2013 and January 2014.

The following items were included in the questionnaire: the type of medical facility, profile of the facility, monthly status of performing prenatal AC and/or MSM testing, involvement of genetic professionals (CGs and/or CGCs) employed, clinical setting for pretest information, staff explaining the tests, an information aid, topics of explanation, time required to provide the information (pre- and post-test) and management of difficult issues. The profile of the facility included the type of the medical facility, total number of deliveries in 2012 and presence of pediatrics. In these questions, we aimed to obtain the answer about the situation at the time of survey.

The statistical software package JMP 11.0.0 (SAS Institute Japan, Tokyo, Japan) was used for all data analyses. The study protocol was approved by the Ethics Committee of Toho University.

RESULTS

The questionnaire response rate was 40.8% (2295/5622). Table 1 includes a summary of the characteristics of the 2295 facilities analyzed. Of these, 864 performed the MSM test (37.7%), 619 performed AC (27.0%) and 412 performed both (18.0%). The number of facilities that involved CGs, CGCs or both were 185 (8.1%), 56 (2.4%) and 197 (8.6%), respectively.

The average number of MSM tests at each institute was 2.0 per month (range 0–52), and 671 of the 864 facilities (77.7%) performed two or fewer MSM tests per month. The average number of AC tests was 2.4 per month (range 0–30), and 438 of the 619 facilities (70.8%) performed two or fewer ACs per month. Table 2 shows a correlation between the performance of prenatal testing and involvement of genetic professionals. The involvement of genetic professionals increased in proportion to the test performance for both tests.

The rate of involvement of genetic professionals in prenatal testing depended on the type of the medical facility. The rates of performing these prenatal tests were lowest in medical clinics without beds (MSM: 130/603 (21.6%) and AC: 25/603 (4.1%)). The MSM test was mostly performed in medical clinics with beds (367/814 (45.1%)) and in perinatal centers (174/393 (44.3%)). The rates of performing AC were also higher in the hospital settings and perinatal centers (203/485 (41.9%) and 225/393 (57.3%), respectively). Involvement of genetic professionals and the number of tests were related to the size of the facility; nevertheless, relatively few facilities employed these specialists (MSM: 96/864 (11.1%) and AC: 128/619 (20.7%)). The higher the medical facility levels, the more genetic professionals were involved.

Participation of a genetic professional lengthened the explanation time compared with that at the facilities without genetic professionals (Table 3). Regardless of the test stage and result, explanations on MSM lasting <30 min were less frequent in the group involving genetic professionals than in that without the professionals (genetic professionals: pretest, 78/96 (79.2%); posttest with a negative screen, 94/96 (97.9%); posttest with a positive screen, 70/96 (72.9%); no genetic professionals: pretest, 748/768 (97.4%); posttest with a negative screen, 754/768 (98.2%); post-test with a positive screen, 689/768 (89.7%)). Similarly, explanations on AC lasting <30 min were less frequent in the group involving genetic professionals than in that without the professionals (genetic professionals: pretest, 94/128 (73.4%); posttest with a negative screen, 126/128 (98.4%); posttest with a positive screen, 58/128 (45.3%); no genetic professionals: pretest, 441/491 (89.8%); posttest with a negative screen, 480/491 (97.8%); posttest with a positive screen, 372/491 (75.8%)).

As shown in Table 4, involvement of genetic professionals enhanced the pretest explanation. Explanation of the MSM test was enhanced on the following items: the method of the procedure, condition(s) of women's complaints, diagnostic test (about AC) and the costs. Regarding AC, the content rates of some topics (condition(s) of women's complaints, conditions that could be diagnosed by AC, ethical issues, termination of pregnancy and the costs) were significantly higher in the genetic professional group.

Among the facilities involving genetic professionals and those not involving them, 533 (69.4%) and 61 (63.5%) facilities, respectively, used an information aid for the MSM test that was made by a clinical laboratory. In addition, the rate of using an information aid that was made by own facilities was significantly higher in the group of genetic professionals than in that not involving them (with genetic professionals: 24/96 (25.0%); no genetic professionals: 97/768 (12.6%)). Of the information aid tools for AC that were used in the facilities involving genetic professionals, 14.1% (18/128) were made in a clinical laboratory and 73.4% (94/128) were made at our own facilities. On the other hand, for explanation of AC, 23.2% of the facilities not involving genetic professionals used a laboratory-made aid and 54.6% used one made at own facility.

Table 5 shows the results of management of difficult issues. To manage difficult issues related to MSM, 53.1% (51/96) of the facilities that involved genetic professionals answered that they could resolve the issues in their own facility. On the other hand, only 16.7% (128/768) of the facilities without genetic professionals dealt with difficult MSM issues on their own. Similarly, for difficult AC issues, 62.5% (80/128) of the facilities with genetic professionals and 25.5% (125/491) of the facilities without the professionals could resolve the issues.

Table 1 Characteristics of the facilities that responded

	All facilities	*Facilities performing MSM*	*Facilities performing AC*	*Facilities performing MSM and AC*
	(n = *2295)*	(n = *864)*	(n = *619)*	(n = *412)*
Type of medical facility				
Medical clinics without beds	603 (26.2%)	130 (15.0%)	25 (4.0%)	16 (3.9%)
Medical clinics with beds	814 (35.5%)	367 (42.5%)	166 (26.8%)	134 (32.5%)
Hospitals without a perinatal care center	485 (21.1%)	193 (22.3%)	203 (32.8%)	145 (35.3%)
Perinatal care center	393 (17.1%)	174 (20.1%)	225 (36.3%)	117 (28.4%)
Number of delivery				
None	920 (40.1%)	195 (22.6%)	45 (7.2%)	32 (7.8%)
1–99	99 (4.3%)	29 (3.4%)	21 (3.4%)	15 (3.6%)
100–499	730 (31.8%)	341 (39.5%)	267 (43.1%)	168 (40.8%)
500–999	347 (15.1%)	203 (23.5%)	201 (32.5%)	138 (33.5%)
1000–1999	69 (3.0%)	45 (5.2%)	62 (10.0%)	40 (9.7%)
Over 2000	4 (0.2%)	4 (0.5%)	4 (0.6%)	4 (1.0%)
NA	126 (5.5%)	47 (5.4%)	19 (3.1%)	15 (3.6%)
Pediatric setting				
Yes without NICU	488 (21.3%)	208 (24.1%)	190 (30.7%)	141 (34.2%)
Yes with NICU	249 (11.8%)	113 (13.1%)	203 (32.8%)	102 (24.8%)
No	1287 (56.1%)	480 (55.6%)	207 (33.4%)	159 (38.6%)
NA	271 (11.8%)	63 (7.3%)	19 (3.1%)	10 (2.4%)
Involvement of clinical geneticists				
Yes	185 (8.1%)	93 (10.8%)	122 (19.7%)	76 (18.4%)
No	2100 (91.9%)	771 (89.2%)	497 (80.3%)	336 (81.6%)
Involvement of certified genetic counselors				
Yes	56 (2.4%)	26 (3.0%)	31 (5.0%)	21 (5.1%)
No	2237 (97.6%)	838 (97.0%)	588 (95.0%)	391 (94.9%)
Involvement of clinical geneticists and/or certified genetic counselors				
Yes	197 (8.6%)	96 (11.1%)	128 (20.7%)	78 (18.9%)
No	2098 (91.4%)	768 (88.9%)	491 (79.3%)	334 (81.1%)
Performance of maternal serum marker tests				
Yes	864 (37.6%)	864 (100%)	412 (66.6%)	412 (100%)
No	1431 (62.4%)	0 (0%)	207 (33.4%)	0 (0%)
Performance of amniocentesis				
Yes	619 (27.0%)	412 (47.7%)	619 (100%)	412 (100%)
No	1676 (73.0%)	452 (52.3%)	0 (0%)	0 (0%)

Abbreviations: AC, amniocentesis; MSM, maternal serum marker; NA, not available; NICU, neonatal intensive care unit.

Table 2 Correlation between involvement of genetic professional and performance of prenatal testing

	Perfomance of maternal serum marker tests[a]		*Perfomance of aminiocentesis*[a]	
Number of cases per month	*Facilities where no GPs were involved* (n = *768)*	*Facilities where GPs were involved* (n = *96)*	*Facilities where no GPs were involved* (n = *491)*	*Facilities where GPs were involved* (n = *128)*
$0 <= n < 1$	498 (64.8)	50 (52.1)	294 (59.9)	30 (23.4)
$1 < n <= 2$	111 (14.5)	12 (12.5)	87 (17.7)	27 (21.1)
$2 < n <= 6$	126 (16.4)	23 (24.0)	91 (18.5)	47 (36.7)
$n > 6$	33 (4.3)	11 (11.5)	19 (3.9)	24 (18.8)

Abbreviation: GP, genetic professionals (clinical geneticists and certified genetic counselors).
[a]There is significant difference among the groups with $P<0.05$ by χ^2 test.

Table 3 Correlation between involvement of genetic professionals and the time required to provide the information on pre- and post-test

	Explanation about maternal serum marker						*Explanation about amniocentesis*					
	Pretest[a]		*Posttest*[a] *(negative screen)*		*Posttest*[a] *(positive screen)*		*Pretest*[a]		*Posttest*[a] *(normal result)*		*Posttest*[a] *(abnormal result)*	
Time required to provide information	*Facilities where no GPs were involved (n = 768)*	*Facilities where GPs were involved (n = 96)*	*Facilities where no GPs were involved (n = 768)*	*Facilities where GPs were involved (n = 96)*	*Facilities where no GPs were involved (n = 768)*	*Facilities where GPs were involved (n = 96)*	*Facilities where no GPs were involved (n = 491)*	*Facilities where GPs were involved (n = 128)*	*Facilities where no GPs were involved (n = 491)*	*Facilities where GPs were involved (n = 128)*	*Facilities where no GPs were involved (n = 491)*	*Facilities where GPs were involved (n = 128)*
<1 min	1 (0.1)	0 (0)	13 (1.7)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	8 (1.6)	5 (3.9)	1 (0.2)	0 (0)
1–4 min	188 (24.5)	14 (14.6)	482 (62.8)	40 (41.7)	77 (10)	3 (3.1)	43 (8.8)	2 (1.6)	333 (67.8)	63 (49.2)	16 (3.3)	2 (1.6)
5–14 min	458 (59.6)	44 (45.8)	236 (30.7)	41 (42.7)	435 (56.6)	36 (37.5)	279 (56.8)	46 (35.9)	123 (25.1)	48 (37.5)	172 (35)	22 (17.2)
15–29 min	101 (13.2)	18 (18.8)	23 (3)	12 (12.5)	177 (23)	31 (32.3)	119 (24.2)	46 (35.9)	16 (3.3)	10 (7.8)	183 (37.3)	34 (26.6)
30–59 min	14 (1.8)	17 (17.7)	4 (0.5)	1 (1)	53 (6.9)	21 (21.9)	42 (8.6)	29 (22.7)	7 (1.4)	2 (1.6)	68 (13.8)	55 (43)
Over 60 min	2 (0.3)	3 (3.1)	0 (0)	0 (0)	4 (0.5)	3 (3.1)	4 (0.8)	5 (3.9)	0 (0)	0 (0)	28 (5.7)	12 (9.4)
NA	4 (0.5)	0 (0)	10 (1.3)	1 (1)	22 (2.9)	2 (2.1)	4 (0.8)	0 (0)	4 (0.8)	0 (0)	23 (4.7)	3 (2.3)

Abbreviations: GP, genetic professionals (clinical geneticists and certified genetic counselors); NA, not available.
[a]There is significant difference among the groups with $P<0.05$ by χ^2 test.

DISCUSSION

To elucidate the status of performing 'conventional' prenatal testing, such as MSM and AC, some studies have been previously conducted, but they were based on the data from clinical laboratories[2,3] or selected facilities.[4] This is the first study that considered Japanese obstetrics/gynecology facilities on a nationwide scale. Thus, we could create a detailed picture of clinical settings for prenatal testing throughout Japan, excluding noninvasive prenatal testing and preimplantation genetic testing.

Involvement of genetic professionals, such as CGs and CGCs, influenced the time required to provide information. Participation of genetic professionals also correlated with the time of explanation. On the basis of the results of some studies conducted outside Japan, the length of prenatal genetic counseling was ~30–45 min.[11,12] Our results showed almost the same tendency as that in the previous Japanese report by Nishiyama *et al.*[13] Because the present study questioned about the time needed to explain genetic testing, not provide genetic counseling, a simple comparison of the duration is slightly difficult. Specifically, some respondents might not have included the assessment of familial history and/or psychological counseling matters in their answers to this question or do not address these issues in their practice. The duration of an explanation was considered to reflect how enhanced the explanation was. Our results prove that genetic professionals contribute to a content-rich explanation and management of difficult issues. Women who participate in prenatal counseling and testing are likely to experience distress and unrealistic perceptions of their risk.[14] Knowledge gained during a prescreening consultation influences pregnant women's attitudes toward further diagnostic testing.[15] We propose to build an education system of perinatal genetic counseling for not only obstetricians but also medical staff that is aimed to improve the informational environment for clients of prenatal diagnosis.

In the present study, <10% of the obstetrics/gynecology facilities involved genetic professionals, despite their contributions. This result demonstrates that most of the pretest information is provided by obstetricians/gynecologists themselves. Because of this, many genetic counseling sessions might not be independent in the context of prenatal testing.

The tradition in prenatal genetic counseling is to provide information and support in a neutral and nondirective manner,[16] but professional training is required.[17] In 2013, the Japanese Association of Medical Sciences (JAMS) and three academic societies associated with medical genetics pointed out that the Japanese model of core curriculum for undergraduate medical education does not have sufficient content for medical genetics education yet.[18] Moreover, in the Japanese medical system, medical genetics is regarded as a subspecialty of other medical specialties and not as an independent specialty. The JAMS recommended that prenatal diagnosis should be conducted after an appropriate genetic counseling session.[19] Active commitment of CGs and CGCs will provide more appropriate genetic counseling for prenatal tests. There may also be a need for creating smooth cooperative networks between the general obstetrics staff and genetic professionals.

However, there is a problem in recruiting perinatal care providers in Japan. Although ~1 million babies are born per year, Japan had 15.6 obstetricians/gynecologists and 40.1 nurse-midwives per 100 000 women in 2011, falling far below the Organization for Economic Cooperation and Development averages of 27.3 and 69.9, respectively.[20] In addition, the number of Japanese CGCs is small, and most CGs work in concurrent positions. The era when whole fetal genome sequencing and the epigenetic status can be obtained will

Table 4 Correlation between dealed topics of pretest explanation and involvement of genetic professionals

	Explanation about maternal serum marker			*Explanation about aminiocentesis*		
Dealed topic in pretest explanation	*Facilities where no GPs were involved* (n = *768*)	*Facilities where GPs were involved* (n = *96*)		*Facilities where no GPs were involved* (n = *491*)	*Facilities where GPs were involved* (n = *128*)	
Method of procedure	571 (74.3)	86 (89.6)	[a]	398 (81.1)	113 (88.3)	
Condition(s) of women's complaint	435 (56.6)	68 (70.8)	[a]	331 (67.4)	106 (82.8)	[a]
Conditions that could be screened by MSM	667 (86.8)	85 (88.5)		455 (92.7)	125 (97.7)	[a]
Ethical issues	320 (41.7)	46 (47.9)		283 (57.6)	93 (72.7)	[a]
Interpretation of the results	626 (81.5)	86 (89.6)		349 (71.1)	109 (85.2)	[a]
Diagnostic test following MSM (MSM only)	646 (84.1)	90 (93.8)	[a]	–	–	
Termination of pregnancy (AC only)	–	–		254 (51.7)	86 (67.2)	[a]
Costs	604 (78.6)	87 (90.6)	[a]	382 (77.8)	112 (87.5)	[a]
Others	19 (2.5)	8 (8.3)	[a]	37 (7.5)	15 (11.7)	

Abbreviations: AC, amniocentesis; GP, genetic professionals (clinical geneticists and certified genetic counselors); MSM, maternal serum marker.
[a]There is significant difference on each item among the groups with $P<0.05$ by χ^2 test.

Table 5 Correlation between the management of difficult issues in the posttest explanation and involvement of genetic professionals

	Explanation about maternal serum marker			*Explanation about aminiocentesis*		
The management of difficult issues	*Facilities where no GPs were involved* (n = *768*)	*Facilities where GPs were involved* (n = *96*)		*Facilities where no GPs were involved* (n = *491*)	*Facilities where GPs were involved* (n = *128*)	
Manage by themselves	122 (15.9)	46 (47.9)	[a]	106 (21.6)	58 (45.3)	[a]
Refer to a specialist in their own hospital	6 (0.8)	5 (5.2)	[a]	19 (3.9)	22 (17.2)	[a]
Refer to another hospital	358 (46.6)	19 (19.8)	[a]	239 (48.7)	24 (18.8)	[a]
Never had a difficult case	272 (35.4)	29 (30.2)		130 (26.5)	23 (18)	[a]
Others	19 (2.5)	2 (2.1)		14 (2.9)	11 (8.6)	[a]

Abbreviation: GP, genetic professionals (clinical geneticists and certified genetic counselors).
[a]There is significant difference on each item among the groups with $P<0.05$ by χ^2 test.

come soon. We consider that the development of human resources in prenatal genetic counseling is an urgent issue in Japan. We should prepare for the coming era that would easily provide fetal comprehensive information.

However, this study had some limitations. Because the response rate was 40.8%, we could not completely ascertain the true representativeness of Japanese obstetricians/gynecologists. Physicians' attitudes toward prenatal testing may have influenced their participation in this study. In addition, some questions, which were developed to summarize event items, such as the time required for explanation, topics of explanation and management of difficult issues, may have raised recall and reporting biases. Because there was variability in the profiles of the facilities and we reviewed the data after dividing the facilities into two groups based on the involvement of genetic professionals, effects of the biases on this research may not be very strong.

Our study proves the challenges faced by Japan in prenatal testing and genetic counseling. There is a need for a discussion of the Japanese system of genetic counseling to provide its further dissemination and raise awareness of this issue to improve prenatal genetic counseling. From the viewpoint of accountability to Japanese society, case registration for prenatal testing would be needed.

This is the first study to highlight the current clinical status of conventional prenatal testing, such as AC and MSM tests, in Japan. Each prenatal test was evaluated depending on the medical facility. Involvement of genetic professionals was found to improve pre- and post-test explanations and posttest management. Active involvement of CGs and CGCs can provide more appropriate genetic counseling for prenatal tests.

CONFLICT OF INTEREST

The authors declare no conflict of interest. This study was funded by the Health Labour Sciences Research Grant (the Japanese Ministry of Health, Labour and Welfare- 201305008A). KK is a former professor of the Department of Obstetrics and Gynecology, Toho University. At the start of this study, KK was working with the Toho University.

ACKNOWLEDGEMENTS

We have greatly benefited from the Japan Association of Obstetricians and Gynecologists (JAOG).

Author contributions: H Miyake, SY, HS, NA, YY, YO, MK, HS, AS, FT, H Masuzaki, YM, FH and KK contributed to the conception, design and composing questionnaire. SY, H Miyake and YF contributed to acquisition of data. KK, SY, H Miyake and YF contributed to the analysis and interpretation of data. H Miyake contributed to drafting of the article. SY, YF, HS, NA, YY,

YO, MK, HS, AS, FT, H Masuzaki, YM, FH and KK contributed to critical revision of the article for important intellectual content. All authors gave final approval of the version to be published.

1 Japan Society of Obstetrics and Gynecology Opinions concerning prenatal genetic testing and diagnosis, (2013). http://www.jsog.or.jp/ethic/H25_6_shusseimae-idengakutekikensa.html. Accessed 27 January 2016. (in Japanese).
2 Matsuda, I. & Suzumori, K. Prenatal genetic testing in Japan. *Community Genet.* **3**, 12–16 (2000).
3 Sasaki, A., Sawai, H., Masuzaki, H., Hirahara, F. & Sago, H. Low prevalence of genetic prenatal diagnosis in Japan. *Prenat. Diagn.* **31**, 1007–1009 (2011).
4 Nishiyama, M., Yan, J., Yotsumoto, J., Sawai, H., Sekizawa, A., Kamei, Y. *et al.* Chromosome abnormalities diagnosed in utero: a Japanese study of 28983 amniotic fluid specimens collected before 22 weeks gestations. *J. Human Genet.* **60**, 133–137 (2015).
5 Ministry of Health, Labour and Welfare Vital Statistics, 2014. (2015) http://www.e-stat.go.jp/SG1/estat/List.do?lid=000001137964. Accessed 27 January 2016. (in Japanese).
6 UNNO, N. The perinatal care system in Japan. *JMAJ* **54**, 234–240 (2011).
7 Wilson, K. L., Czerwinski, J. L., Hoskovec, J. M., Noblin, S. J., Sullivan, C. M., Harbison, A. *et al.* NSGC practice guideline: prenatal screening and diagnostic testing options for chromosome aneuploidy. *J .Genet. Couns.* **22**, 4–15 (2013).
8 Centers for Disease Control and Prevention. Chorionic villus sampling and amniocentesis: recommendations for prenatal counseling. *MMWR* **44**, 1–12 (1995).
9 Ministry of Health, Labour and Welfare Survey of Medical Institutions, 2014. (2015) http://www.mhlw.go.jp/toukei/saikin/hw/iryosd/14/dl/1-1.pdf. Accessed 27 January 2016. (in Japanese).
10 Sago, H., Sekizawa, A. & Japan NIPT consortium. Nationwide demonstration project of next-generation sequencing of cell-free DNA in maternal plasma in Japan: 1-year experience. *Prenat. Diagn.* **35**, 331–336 (2015).
11 Bernhardt, B. A., Geller, G., Doksum, T., Larson, S. M., Roter, D. & Holtzman, N. A. Prenatal genetic testing: content of discussions between obstetric providers and pregnant women. *Obstet. Gynecol.* **91**, 648–655 (1998).
12 Meiser, B., Irle, J., Lobb, E. & Barlow-Stewart, K. Assessment of the content and process of genetic counseling: a critical review of empirical studies. *J. Genet.* **17**, 434–451 (2008).
13 Nishiyama, M., Sawai, H. & Kosugi, S. The current state of genetic counseling before and after amniocentesis for fetal karyotyping in Japan: a survey of obstetric hospital clients of a prenatal testing laboratory. *J. Genet. Couns.* **22**, 795–804 (2013).
14 Tercyak, K. P., Johnson, S. B., Roberts, S. F. & Cruz, A. C. Psychological response to prenatal genetic counseling and amniocentesis. *Patient Educ. Couns.* **43**, 73–84 (2001).
15 Brajenović-Milić, B., Babić, I., Ristić, S., Vraneković, J., Brumini, G. & Kapović, M. Pregnant women's attitudes toward amniocentesis before receiving Down syndrome screening results. *Womens Health Issues* **18**, 79–84 (2008).
16 World Health Organization WHO Review of ethical issue of medical genetics, 2003. (2003) http://www.who.int/genomics/publications/en/ethical_issuesin_medgenetics%2Oreport.pdf. Accessed 27 January 2016.
17 Korf, B. R. & Irons, M. B. *Human Genetics and Genomics* 4th edn (Wiley-BlackBlackwell, West Sussex, UK, 2013).
18 Japanese Association of Medical Sciences, The Japan's National Liaison Council for Clinical Sections of Medical Genetics, The Japan Society of Human Genetics, Japan Society for Genetic Counseling. Model curriculum for undergraduate medical genetics education, 2013. (2013) http://jshg.jp/news/data/news_130422.pdf. Accessed 27 January 2016. (in Japanese).
19 The Japanese Association of Medical Sciences Guidelines for Genetic Tests and Diagnoses in Medical Practice, 2012. (2012) http://jams.med.or.jp/guideline/genetics-diagnosis_e.pdf. Accessed 27 January 2016.
20 Fukuzawa, R.K. & Kodate, N. in *Maternity Services and Policy in an International Context: Risk, Citizenship and Welfare Regimes* (eds Kennedy P. & Kodate N.) 153–178 (Routledge, London, UK, 2015).