ORIGINAL ARTICLE

A survey of prenatal first-trimester aneuploidy screening among Hong Kong specialist obstetricians

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Objectives To determine the background, qualifications, and certification status of specialists currently performing first trimester screening in Hong Kong, the extent of their participation (and the laboratories they use) in quality assurance programmes, and their willingness to provide follow-up data for auditing purposes.

Design Questionnaire survey.

Setting Hong Kong.

Participants A survey was mailed to all registered Hong Kong specialist obstetricians. Results were reported using descriptive statistics.

Results The response rate was 32% (106/331). Overall, 73% offered universal screening to all pregnant women. The majority (72%) most commonly performed first trimester screening for their patients. Sixty-six (62%) of the respondents performed nuchal translucency scanning; only 30 (45%) were accredited by a recognised body to perform such scans. Only 33% of the relevant laboratories used by specialists participated in external quality assurance programmes specific to Down's syndrome screening undertaken by a third party organisation.

Conclusions According to our data, first trimester screening has become one of the most common screening strategies for Down's syndrome in Hong Kong, but there is a need to assess the quality of such prenatal screening for aneuploidy to ensure its efficacy.

Introduction

In many nations prenatal screening for foetal aneuploidy has become an integral part of the modern antenatal care, and many professional bodies suggest that such testing should be available to all pregnant women.[1,2] Over the past few decades, many screening strategies have been developed. Most commonly they entailed: second-trimester biochemical testing, first-trimester nuchal translucency (NT) testing, first-trimester combined NT and biochemical testing, and integrated first and second trimester testing. Each strategy has its own merits in terms of sensitivity, false-positive rates, training programmes, quality control requirements and complexity. Over the last 5 years, first-trimester combined screening has become one of the most commonly used, because of its high detection rate and the facility with which the whole test can be completed in one single visit during the first trimester.[3]

It is well known, however, that the performance of these prenatal aneuploidy screening tests is affected by many factors. This is particularly true of first trimester screening, which includes both NT scan and biochemical assays for free beta-human chorionic gonadotrophins (f-bhCG) and pregnancy-associated plasma protein A (PAPP-A). The NT scan is a highly operator-dependent procedure, and reliable results can be expected only if it is performed by well-trained, certified sonographers who also undergo regular quality control and auditing.[4] Similarly, there are many pre-analytical and analytical factors which significantly affect the reliability of the biochemical assays for f-bhCG and PAPP-A. Therefore, any laboratory providing such services should follow strictly recommended standards and undergo stringent and regular internal and external quality assurance (QA) assessments.[5] In Hong Kong, the number of specialist obstetricians and laboratories providing first trimester screening tests has increased over the last few years. It is unclear, however, how many of these specialists are fully trained and certified to perform NT scans, and to what extent, if any, the laboratories performing relevant biochemical analysis participate in both internal and external QA programmes.

Key words
Down syndrome; Mass screening; Nuchal translucency measurement; Pregnancy trimester, first; Quality assurance, health care

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關於香港產科醫生進行妊娠早期非整倍體篩查的一項調查

目的 探討進行妊娠早期非整倍體篩查的香港產科醫生的背景、學歷、專業資格、使用實驗室參與質量保證計劃的程度，以及是否願意提供隨訪資料以作評核用途。

設計 問卷調查。

安排 香港。

參與者 向所有香港註冊的產科醫生發放問卷，並用描述統計分析所得結果。

結果 回應率為32%（106/331）。受訪醫生中，73%會為所有孕婦提供篩查。大部份醫生（72%）都作妊娠早期篩查。66位（62%）受訪醫生會進行胎兒後頸皮下透明層掃描；但只有30位（45%）被指定機構獲頒發認可進行此項掃描。受訪醫生使用的實驗室中，只有33%參與有第三者組織保證的唐氏綜合徵篩查質量保證計劃。

結論 根據本調查數據，妊娠早期篩查已成為香港針對唐氏綜合徵的其中一種最普遍篩查策略，唯仍須評估此產前篩查的質量，以確保其效用。

The objectives of this study were to determine: (1) the background, qualifications, and certification status of specialists currently offering and performing prenatal aneuploidy screening tests in Hong Kong, (2) the extent of participation of local specialists and laboratories in internal and external QA programmes, and (3) the willingness of Hong Kong specialists to provide follow-up data of individual woman screened if requested by third party laboratories for auditing purposes.

Methods

A survey was mailed to all specialist obstetricians in Hong Kong. The names and registered contact addresses of all specialist obstetricians (Fellows of the Hong Kong College of Obstetricians and Gynaecologists) were extracted from the website of the Medical Council of Hong Kong, which is publicly listed and freely available. A letter of invitation to participate in the study was sent to each specialist along with the survey form. The invitation explained the purpose of the study and that participation was voluntary and all information would remain anonymous. Those consenting to participate in the study were asked to complete the survey and return the completed questionnaire to the study coordinator using the accompanying stamped, self-addressed envelope within 1 calendar month. The whole study was approved by the Chinese University of Hong Kong Survey and Behavioural Research Ethics Committee.

The survey was composed of three sections. The first elicited background information of the specialists, including years and type of practice. The second elicited the screening practice for aneuploidy among specialists, including whether they performed the screening, the method used, and the type of patients they screened. The third section elicited screening practice in the first trimester, including whether they performed NT scans and whether such screening had entailed any formal training.

Questionnaires not returned within 1 calendar month were excluded from the analysis. Descriptive statistics were used to report the results. Between-group comparisons were performed using the Chi squared test or unpaired sample *t* tests where appropriate.

Results

Of 331 questionnaires sent off, 106 (32%) responded. The mean duration of practice in obstetrics and gynaecology for the responding specialists was 22 years. Among the respondents, 22%, 5%, 3%, and 2% were recognised subspecialists in maternal and foetal medicine, reproductive medicine, urogynaecology, and gynaecological oncology, respectively.

In all, 73 (69%) and 33 (31%) were practising in the private and public sectors, respectively. Table 1 shows the basic characteristics and practice patterns in prenatal screening and diagnosis for foetal Down's syndrome. Respondents working in private institutions had significantly longer professional working experience (24 vs 17 years) but a lower percentage of subspecialists in maternal and foetal medicine (14% vs 39%). Significantly more respondents from the private sector (88% vs 39%) offered universal Down's syndrome screening to all their patients. Almost 40% of respondents from the public sector only offered a screening test to patients classified as being of 'advanced maternal age' while only 1% of respondents from the private sector did so. On the other hand, there was no difference between the two groups of doctors with respect to the screening test they would offer when needed; over 90% offered first trimester screening, and over 80% also discussed second trimester screening. However, there was a significant difference in terms of the actual screening test they performed; first trimester screening was used in 82% of the patients in the private sector compared to 48% among those in the public sector. When a prenatal diagnosis is required, significantly more public specialists used karyotyping alone (42% vs 8%), while the majority of private specialists (74%) used both formal karyotyping and rapid karyotyping based on polymerase chain reactions or fluorescence in-situ hybridisation. For both groups of doctors, 65% would follow up data on pregnancy outcome of all the women that had been

TABLE 1. Preferences for prenatal screening and diagnosis of foetal Down's syndrome among the respondents*

	Overall (n=106)	Type of practice		P value
		Private (n=73)	Public (n=33)	
Mean (±standard deviation) duration of practice in obstetrics and gynaecology (years)	22±9	24±9	17±6	<0.001
Subspecialist in maternal and foetal medicine	23 (22%)	10 (14%)	13 (39%)	0.003
Offer screening test to all patients (universal screening)	77 (73%)	64 (88%)	13 (39%)	<0.001
Offer screening test to patients of advanced maternal age only	13 (12%)	1 (1%)	12 (36%)	<0.001
Include first trimester screening test in their offer	97 (92%)	67 (92%)	30 (91%)	0.881
Include second trimester screening test in their offer	89 (84%)	62 (85%)	27 (82%)	0.686
The commonest screening method actually used				
First-trimester combined	76 (72%)	60 (82%)	16 (48%)	<0.001
Integrated	20 (19%)	9 (12%)	11 (33%)	0.010
Second-trimester biochemical	7 (7)	3 (4%)	4 (12%)	0.124
Diagnostic test used in the majority of cases				
Karyotyping only	20 (19%)	6 (8%)	14 (42%)	<0.001
Karyotyping + PCR/FISH†	71 (67%)	54 (74%)	17 (52%)	0.023
Follow-up for pregnancy outcome				
All cases	69 (65%)	46 (63%)	23 (70%)	0.561
Screened positive cases only	10 (9%)	7 (10%)	3 (9%)	0.935

* Between-group comparisons were performed by either unpaired *t* test or Chi squared test as appropriate

† PCR denotes polymerase chain reaction, and FISH fluorescence in-situ hybridisation

screened, while only 9% attempted to obtain follow-up data in patients classified as high risk by their screening.

Among the 106 respondents, 66 performed first-trimester NT scans themselves. Of these, 30 were certified and accredited to perform NT scans, 35 were not, and the certification status of one was unknown. Table 2 shows the practice details of first trimester screening among the specialists. Those who were accredited performed significantly more NT scans per month than those who were not. All accredited respondents performed the NT scan at the correct gestational age, while 23% of uncertified respondents performed them outside the recommended range of 11-13+6 weeks (+6 refers to days). Some of the latter scans were performed as early as 8 weeks and as late as 20 weeks. All accredited respondents had received formal training on NT scan (a prerequisite for certification), while only 66% of the uncertified respondents had received such training. Almost all those who performed NT scans included biochemical tests as part of their screening protocol. Overall, more than 1800 first trimester screening tests were performed per month by these 66 respondents, corresponding to about 22 000 tests per annum.

There were 64 respondents who used first-trimester combined NT scans performed the test themselves and employed biochemical screening in addition. Table 3 shows the biochemical testing details. The majority (88%) used an external laboratory for the biochemical assays. Approximately 28% and 64% of the respondents respectively did not know whether the laboratory they were using was subject to regular internal QA assessment or had participated in an external QA programme. All, except five, agreed to provide patient follow-up data to the laboratory to conduct QA for the screening programme.

TABLE 2. Practice details of first trimester screening among those who performed nuchal translucency (NT) scans themselves, according to certification status of doctor

Details	Certification status		P value
	Yes (n=30)	No (n=35)	
Median numbers of NT scans performed per month	21-50	6-10	0.011
Range of gestational age for NT assessment			
Correct (11-13+6 weeks)	30 (100%)	27 (77%)	0.020
Start at <11 weeks	0	6 (17%)	
Start at <11 weeks and up to >14 weeks	0	2 (6%)	
Had received formal training on NT scan	30 (100%)	23 (66%)	0.000
Include biochemistry on top of NT in the screening test	30 (100%)	34 (97%)	1.000

All those who measured NT outside the recommended gestational age used biochemical laboratories not requiring certification in NT measurement.

Discussion

Our results showed that there was significant

TABLE 3. Biochemical testing details for those undertaking first-trimester combined (nuchal translucency + biochemistry) screening tests (n=64)

Details	No. (%) of participants
Locate of biochemical laboratory	
Own laboratory	8 (13)
External laboratory	56 (88)
Does your laboratory conduct regular internal quality assurance exercise?	
Do not know	18 (28)
No	0
Yes	46 (72)
Does your laboratory participate in any external quality assurance programme?*	
Do not know	41 (64)
No	2 (3)
Yes (not specified)	9 (14)
Yes (FMFUK)	9 (14)
Yes (UKNEQAS)	3 (5)
Do you agree to provide patient follow-up data to the laboratory for quality assurance?†	
No	2 (3)
Yes	59 (92)

* FMFUK denotes Fetal Medicine Foundation of the United Kingdom, and UKNEQAS United Kingdom National External Quality Assessment Service

† No answers were given for three participants

difference in the practice of prenatal screening and diagnosis of foetal Down's syndrome between public- and private-sector specialists in Hong Kong. Although the Hong Kong Hospital Authority is still only offering second-trimester biochemical screening or invasive testing to women aged 35 years or above and no formal testing for younger subjects, close to 40% of public specialists discussed screening tests with all pregnant women, and over 90% included first trimester screening in their counselling. Among the private specialists, almost 90% practised universal screening for all pregnant women, and over 90% include first trimester screening in the counselling. Overall, 66 of the respondents performed NT screening themselves, which extrapolates to about 22 000 per annum. The actual number was likely to be higher, as only 32% of known specialists completed this questionnaire survey. Given that there are about 60 000 annual deliveries in Hong Kong, it is obvious that first-trimester Down's syndrome screening has become common in Hong Kong.

Our results showed that about half (35/65) of those performing NT scans were not certified. Screening by NT needs to be very precise. The average NT between 11-13+6 weeks of gestation is about 1.5 mm, and a measurement error of -0.2 mm will already lead to an important change in the false-negative rate.[6] Proper training with certification and adherence to standard protocols is to ensure that NT is measured correctly[7] and increase the detection rate of foetal Down's syndrome from approximately 34 to 84%.[8] It is therefore important that those who perform such scans are appropriately trained, accredited, and be subject to regular auditing for re-certification at yearly intervals.[9] Regrettably, more than 50% of specialists who perform NT scans in Hong Kong are not certified, and among these as many as 23% carried out the measurement outside the recommended gestation range of 11-13+6 weeks. Alarmingly, sometimes NT was measured as early as 8 weeks and as late as 20 weeks. The standard protocol for NT screening originally developed by the Fetal Medicine Foundation of the United Kingdom (FMFUK) has now been widely adopted as the global standard. In addition to the FMFUK, there are many national bodies in many western countries that provide training and certification in NT scan.

The quality of the biochemical assays is also very important in foetal Down's syndrome screening. A small increase in assay variation can have a significant effect on risk estimation.[10,11] This is particularly important for first trimester markers, namely f-bhCG and PAPP-A, which are particularly prone to pre-analytical and analytical variations. Therefore, both regular internal QA and participation in external QA programmes such as the United Kingdom National External Quality Assessment Service (UKNEQAS) are essential. Moreover, appropriate accreditation should be maintained. Furthermore, quality assessment must be specific to first trimester screening, rather than a general accreditation scheme. For example, many laboratories in Hong Kong claimed that they are ISO 15189– and HOKLAS- (Hong Kong Laboratory Accreditation Scheme) compliant, which only recognises a laboratory's capability in performing specific tests that they applied for, but not necessarily for the first trimester screening test. One of the most important effects of proper accreditation of laboratories is that they only accept blood samples sent by specialists who are certified to perform NT scans, thereby increasing the likelihood that all measurements are reliable for risk calculation. To the best of our knowledge, at least half of the laboratories in Hong Kong that provide risk estimation in the first trimester are not accredited, and accept NT measurements from uncertified specialists. This poses a significant threat to the reliability and efficacy of their test results.

Ultimate confirmation that a screening programme is effective and successful depends on complete follow-up data of pregnancy outcomes, and the documented false-negative and true-positive rates. Each individual specialist should be assessed, as should the relevant biochemical laboratories. It is encouraging that about 65% of the respondents

indicated that they had complete follow-up of all the subjects they had screened, and that over 90% were agreeable to providing patient follow-up data to the biochemical laboratory for QA if asked. Without such meticulous follow-up, it would not be easy to identify any problems in a screening programme, and thus avoid unnecessary suffering to patients.

In conclusion, the first trimester screening strategy has become one of the most commonly used prenatal Down's syndrome screening strategies in Hong Kong. However, many specialists are performing NT assessment without proper training and certification, and many laboratories are not accredited and calculate risks based on NT measured by uncertified specialists. Such practice is unacceptable in most developed countries, where all specialists who perform NT must be properly trained and certified.

Our data indicate that there is a need for assessment of the quality of prenatal screening in order to ensure that the efficacy of screening for aneuploidy is maintained and that those performing prenatal screening tests report the outcomes of corresponding pregnancies. Mechanisms to facilitate the collection and auditing screened pregnancies need to be established.

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