Detection of foetal anomaly in advanced maternal age

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ABSTRACT

Objective: The aim of this study was to assess the prevalence of foetal anomaly diagnosed during a detailed ultrasonography amongst patients of advanced maternal age (AMA) and to identify the related anomalies in these age groups.

Method: A retrospective observational study amongst AMA mothers was done in Universiti Kebangsaan Malaysia Medical Centre, a Malaysian teaching hospital. The data over a period of three years (January 2013 – December 2016) obtained from the Maternal Foetal Medicine clinic registry was analysed. AMA mothers with singleton pregnancy presenting for foetal structural anomaly scan was included. They were later subdivided into 2 groups (35-39 years and ≥ 40 years). The logistic regression analysis was used to analyse the association of the chromosomal anomalies and the age groups.

Results: In all 486 patients were recruited and 84 patients were identified with foetal anomaly (17.3%). There was no significant difference in the prevalence of foetal anomalies or significant association with a specific structural foetal anomaly identified (p>0.05). However, the number of follow-ups for these patients are significantly higher (p<0.001).

Conclusion: The prevalence of structural foetal anomalies identified in detailed ultrasonography was low in AMA mothers. Hence, referral criteria for detailed anomaly ultrasonography need to be re-looked.

KEYWORDS:
Advanced maternal age, foetal anomaly, detailed foetal ultrasonography

INTRODUCTION

Childbearing above the age of 35 years old regardless of their parity is considered to be at an advanced maternal age (AMA). There has been an increase in number of pregnancies reported amongst women of advanced maternal age in the past two decades.[1] This increase is also seen amongst women in the high-income countries.[2] Many studies have also reported an association between AMA and higher outcome of adverse maternal and foetal outcome.[3-5]

Some of the adverse effects are low birth weight, preterm deliveries, stillbirth and unexplained foetal death.[6-11] Apart from these, the devastating effects of chromosomal and structural abnormalities are well known correlations.[12]

However, in recent years, studies have suggested that younger maternal age (19 years and less) may have a stronger risk factor resulting in congenital anomalies in comparison with AMA.[13,14] Many studies are now directed towards this. Nevertheless, we are still lacking data in our local population with limited resources available.

Most of the Maternal Foetal Medicine services in Malaysia screen patients from the AMA for structural anomalies from 18 weeks of gestation. However, the numbers are on a rise due to increasing rates of AMA mothers embarking in pregnancy. Against this background, the aim of this study was to examine the prevalence of structural anomalies amongst the AMA and to deduce the ideal AMA group patients who would benefit from screening. This would serve as a basis to concentrate on these particular groups in hospitals with limited resources and to reduce the number of unnecessary referrals to tertiary hospitals with a Maternal Foetal Medicine speciality.

MATERIALS AND METHODS

Study design

This was a retrospective observational study. This study was conducted in the Universiti Kebangsaan Malaysia Medical Centre (UKMMC), a tertiary teaching hospital, in the Department of Obstetrics and Gynaecology. Data over the period of three years (January 2013-December 2016) was obtained from the Maternal Foetal Medicine Registry of UKMMC. Approval from the UKM Research Ethics Committee was obtained (FF-2017-456).

The inclusion criteria were all mothers above ≥35 years old at the time of foetal anomaly ultrasonography with a singleton gestation. The mother had to undergo at least one foetal anomaly ultrasonography by the team in Maternal Foetal Medicine Unit who is credentialed to perform foetal anatomical survey. The exclusion criteria were patients aged below 35years old and multiple gestation.

Those participants who were included in the study was further subdivided into two age groups, i.e., 35-39 years and ≥40 years. Maternal demographic information and obstetrical history was entered in the database. Foetal anomalies identified were also included in the database for further analysis.

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Table I: Maternal ethnicity and foetal anomaly

Variable	Foetal anomaly in age group 35-39 years		P value	Foetal anomaly in age group ≥40yrs		p value
	Yes	No		Yes	No	
Malay	51	254	0.747	12	57	0.291
Chinese	12	63		7	13	
Indian	2	7		0	2	
Others	0	5		0	1	

*Pearson chi-square was applied for categorical data. p-value of <0.05 is significant.

Table II: Maternal parity and foetal anomaly

Variable	Age group 35-39 years	Age group ≥40yrs	P value
Parity 0	62 (15.7%)	9 (9.8%)	0.058
Parity 1-5	327 (83.0%)	79 (85.9%)	
Parity >5	5 (1.3%)	4 (4.3%)	

*Chi-Square test

Table III: Foetal structural anomaly identified in the compared group

Variable	n	Age 35-39yrs	Age ≥40yrs	OR (95%CI)	aOR (95%CI)	P Value
Nervous systems	13 (2.67%)	10 (2.54%)	3 (3.26%)	1.294 (0.349, 4.800)	1.133 (0.296, 4.334)	0.855
Urinary system	11 (2.26%)	8 (2.03%)	3 (3.26%)	1.626 (0.423, 6.253)	2.295 (0.572, 9.212)	0.241
GIT	19 (3.91%)	16 (4.06%)	3 (3.26%)	0.796 (0.227, 2.792)	0.808 (0.224, 2.923)	0.746
Limbs	6 (1.23%)	5 (1.27%)	1 (1.09%)	0.855 (0.099, 7.407)	1.152 (0.129, 10.256)	0.899
Hearts	26 (5.35%)	19 (4.82%)	7 (7.61%)	0.289 (0.662, 3.990)	1.601 (0.639, 4.011)	0.315
Others	30 (6.17%)	21 (5.33%)	9 (9.78%)	1.926 (0.851, 4.357)	1.989 (0.861, 4.595)	0.107

[a]Adjusted for ethnicity and parity. Logistic regression analysis was used. p-value of <0.05 is significant.
Note: The findings might be overlapped in a single patient.

Table IV: Association between foetal structural anomaly versus follow-ups

Variable		Foetal anomaly in age group 35-39 years		P value	Foetal anomaly in age group ≥40yrs		p value
		Yes	No		Yes	No	
Follow up	Yes	24	14	<0.001	12	0	<0.001
	No	41	315		7	73	

Pearson chi-square was applied. p-value of <0.05 is significant.

Table V: Association foetal anomaly identified versus amniocentesis

		Foetal anomaly in age group 35-39 years		P value	Foetal anomaly in age group ≥40yrs		p value
		Yes	No		Yes	No	
Amniocentesis done	Not done	59	326	<0.001	14	72	0.001
	Done	6	3		5	1	
Results	Normal	2	2	0.810	4	1	0.667
	Abnormal	4	1		0	1	

Pearson chi-square was applied. p-value of <0.05 is significant.

The primary outcome was to assess the prevalence of foetal anomalies diagnosed during the detailed ultrasonography. Structural anomalies were categorised by organ systems such as central nervous system, genitourinary system, gastrointestinal system, cardiovascular and musculoskeletal.

The secondary outcome of the study was to determine the relationship between foetal anomalies and the AMA, hoping to establish any particular system involved as per the age groups subdivided. Our hypothesis was that prevalence of foetal anomalies was higher with increasing maternal age.

Statistical analysis

The baseline maternal characteristics and the prevalence of chromosomal abnormalities between groups were compared using Chi square test and Mann-Whitney test. The logistic regression analysis was used to analyse the association of the prevalence of chromosomal anomalies and the subdivided age groups. All collected data were analysed using IBM Statistical Package for Social Science (SPSS) version 25. A p value <0.05 was considered statistically significant.

RESULTS

Four hundred and eighty-six women were included in our study where 394 women were in the age group of 35-39 years and the remaining 92 women were ≥40 years. The majority of patients were from the Malays 76.9%, followed by Chinese 19.5% and the Indians 2.2%, most likely due to catchment area, and this distribution concurs with the demographic breakdown of ethnicity in Malaysia (Table I)

As per our data, the patients from parity 1-5 were the largest number referred for detail anomaly scan and most of them belonged to the age group 35-39 years of age.

Mothers in their first pregnancy ≥40 years were nine patients comprising 9.8% of the same age group and 1.8% of the entire sample size. There is no statistical significance of AMA with the parity (Table II).

Eighty-four patients were identified with foetal anomalies, 65 patients of age group 35-39 years, i.e., 13.3% and 19 (3.9%) in ≥40 years group. There is no significant difference in the numbers seen in both groups.

Most of the foetal anomalies were noted in the cardiovascular system out of which 20 were identified having echogenic foci in the ventricles. Three had ventricular septal defect, one with tetralogy of Fallot and two with pericardial effusion.

The most common abnormality in the gastrointestinal system was the presence of hyperechoic bowel. This was identified in 16 patients and the remaining three were dilated bowel.

Nine foetuses were identified to have dilated renal pelvic calyces, one with suspected dysplastic kidney and one foetus was identified to have hydrocele.

As for the central nervous system, two foetuses were noted to have choroid plexus cyst, two foetuses with ventriculomegaly, one with a Blake's pouch cyst, two with absent of the vermis, three with enlarged cisterna magna and three had thickened nuchal fold.

There were six foetuses with shortening of the limbs and one with congenital talipus. Ten foetuses were identified to have abnormalities in more than one system. The distribution of anomalies by organ systems in both the AMA groups showed no significant association in the two groups (Table III)

There is a significant difference between follow up and structural anomaly status. Patients with identified foetal anomaly required more follow-up as they require further evaluation, counselling and plan (Table IV).

The patients who required further follow up to the Maternal Foetal Medicine Unit after structural anomaly identified was 42.8%, hence increasing the workload of the clinic further.

Even though there were four hundred and eighty-six patients recruited in this study, only 15 patients agreed for amniocentesis. The causes of this low uptake were unfortunately not documented in the registry (Table V).

DISCUSSION

AMA is reported to be associated with decrease in the risk of major congenital abnormalities in the absence of aneuploidy.[15] There is a four -fold increase in the risk of chromosomal abnormalities in older women. In comparison to mother in the age 25-29 years old, the mother above 35 years was four to seven times greater in foetuses having chromosomal abnormalities.[16] Our study similarly demonstrates that the prevalence of foetal anomalies was low despite the large group of patients screened (17.3%) with 2.04% having foetal anomalies involving more than one system. Hence, chromosomal and genetic disorders require screening that is more stringent rather than structural survey of foetus in AMA mothers. This is an important point that should be considered when deciding on methods of screening of all AMA mothers.

Based on the findings in our study, perhaps we should be looking at other methods of screening AMA mothers, since the prevalence of structural anomalies is not significantly higher. Therefore, there should be a shift in screening patients for structural anomaly to a more aggressive screening of aneuploidy by NICC or amniocentesis.

Amniocentesis even though invasive is relatively safe and more so in the hands of well-trained Maternal Foetal Medicine specialists. The risk of infection, i.e., chorioamnionitis is less than 0.1%. The rate of foetal lost related to amniocentesis is also low at around 0.5%. In our study, the number of patients that agreed for amniocentesis was low whereby only 15 patients agreed for the test in spite of a large number of 486 patients: undergoing foetal anomaly ultrasonography. Issues related to affordability, cultural, religious, or even poor counselling needs to be analysed to identify the reason. Unfortunately, the reason for refusal was unavailable in our data to make a conclusion.

In the recent years, cell free foetal DNA technology being a non-invasive test may be an option to consider in screening for aneuploidy in AMA mothers. In case where the test was abnormal, an amniocentesis is still required for confirmation. Bianchi et al. 2014 reported that invasive testing managed to identify 93% of trisomy 21, 64% with trisomy 18, 44% with trisomy 13 and 38% with sex chromosomal abnormalities in those with abnormal cell free foetal DNA results.[19] Hence, more studies looking into these choices of screening in AMA mothers may be more beneficial.

The age of screening pregnant mothers with a foetal anomaly ultrasonography is not standardised across the globe, similar discrepancies in different centres in Malaysia were also recognised. This may be due to the lack of expertise or the high load of cases in the tertiary centres making individual screening criteria different. In our study, we attempted to identify the ideal screening age group amongst the AMA mothers, hoping to concentrate more on these groups of mothers. Unfortunately, in our study, we could not identify the ideal age for screening AMA mothers for foetal anomalies as well as establish any relationship between foetal anomalies and the subdivided AMA groups. Perhaps future studies will guide us to identify the ideal age and focus on targeted systems.

Counselling is essential to ensure the patients truly understand the significance and importance of screening. Any doubts and uncertainties should be tackled during those sessions. The difference of screening for structural anomalies and chromosomal abnormalities, as well screening versus confirmatory test needed to be explained for further understanding. This may help patients being more willing for NICC or improve the uptake of amniocentesis if required as the uptake is rather poor based on our study. The primary care centres play a pivotal role in counselling, as the initial encounter with patients starts here.

This will significantly reduce the major bulk of the referrals for AMA to our Maternal Foetal Medicine Specialist and enable other high-risk obstetrics case to be given the importance. Indirectly improving the quality of care of these patients.

Our study has limitations, including its retrospective nature, being from a single tertiary centre and newer advances that may not be available in Maternal Foetal Medicine practice during the study period. More multi-centred studies are required to explore the ideal method and age groups for screening AMA mothers hoping to improve the quality of care for these women. More study on NICC and amniocentesis amongst AMA may also be beneficial. We hope that in future an appropriate screening will avail for these AMA mothers.

CONCLUSION

The prevalence of structural foetal anomalies identified in detailed ultrasonography was low in AMA mothers.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest. The authors alone are responsible for the content and the writing of the paper.

ETHICAL APPROVAL

The study was approved by the UKM Research Ethics Committee was obtained (FF-2017-456).

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