Women's age and total motile normal morphology sperm count predict fecundability: a prospective cohort study

Mei Ting Lam ,[1,2] Hang Wun Raymond Li ,[1,2,3] Ching Yin Grace Wong,[1,3] William Shu Biu Yeung,[1] Pak Chung Ho,[1] Ernest Hung Yu Ng[1,2]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmjsrh-2020-200639).

[1]Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong
[2]Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Yau Ma Tei, Hong Kong
[3]The Family Planning Association of Hong Kong, Wan Chai, Hong Kong

Correspondence to
Dr Mei Ting Lam, Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Yau Ma Tei, Hong Kong; lmt256@ha.org.hk

Received 10 March 2020
Revised 10 June 2020
Accepted 14 June 2020
Published Online First 27 July 2020

Linked

► http://dx.doi.org/10.1136/bmjsrh-2020-200762

To cite: Lam MT, Li HWR, Wong CYG, *et al*. *BMJ Sex Reprod Health* 2020;**46**:279–286.

ABSTRACT

Objective This study investigated the role of women's age, serum anti-Müllerian hormone (AMH) level and semen parameters in predicting fecundability.

Methods This was a prospective cohort study on couples attending for preconceptional health check. Occurrence of conception at 1 year after ceasing contraception and time to pregnancy were noted by telephone follow-up. The women's age, serum AMH level and total motile normal morphology sperm count (TMNC) were compared between those who conceived and those who did not after 1 year; their independent predictive value on conception at 1 year was analysed by logistic regression. Among those conceiving within 1 year, Spearman's correlations between time to pregnancy and the clinical parameters were studied.

Results Of the 100 couples analysed, we found younger age of the women (p=0.008), higher serum AMH level (p=0.038) and higher TMNC (p=0.015) in those that conceived within 1 year. Multivariate logistic regression found that women's age (OR 0.867, 95% CI 0.761 to 0.988, p=0.032) and TMNC (OR 1.089, 95% 1.001–1.185, p=0.047), but not serum AMH level, significantly predicted conception within 1 year. Among those that conceived within 1 year, none of the parameters analysed were correlated with time to pregnancy within 1 year.

Conclusions Women's age and TNMC are significant independent predictors of conception within 1 year. No parameter was shown to predict the time to pregnancy within 1 year. This finding can aid preconceptional counselling of couples who are planning for pregnancy.

Key messages

- Women's age and total motile normal morphology sperm count, but not serum anti-Müllerian hormone level, were significant independent predictors of conception within 1 year.
- Lower high-density lipoprotein cholesterol levels in the female and male were found in couples that conceived within 1 year, but the magnitude of difference was very small.
- In our cohort, couples conceiving within 1 year or those who did not showed no differences in men's age, body mass index, other lipid parameters, physical activity and stress score.

INTRODUCTION

Fecundability is the probability of a pregnancy, during a single menstrual cycle in a woman with adequate exposure to sperm and no contraception, culminating in a live birth.[1] Time to pregnancy is the time taken to establish a pregnancy, measured in months or in numbers of menstrual cycles.[1] There is a trend towards delaying childbearing, resulting in more women facing fertility problem at the time they hope to conceive.[2] If the factors affecting fertility could be identified, it might be possible to offer counselling on family planning and possible early fertility intervention. Various factors have been studied for their influence or predictive value on fecundability, particularly those related to the production and competence of gametes, such as women's age and serum anti-Müllerian hormone (AMH) level as well as semen parameters.

Table 1 Comparison of study participants' basic demographic and clinical parameters between those couples that conceived within 1 year and those that did not

Parameter		Overall	Conception within 1 year		P value
			Yes (n=61)	No (n=39)	
Coital frequency at recruitment	≥2 per week	24 (24)	14 (23.0)	10 (25.6)	0.824
	1 per week	36 (36)	23 (37.7)	13 (33.3)	
	1–3 per month	35 (35)	20 (32.8)	15 (38.5)	
	<1 per month	5 (5)	4 (6.6)	1 (2.6)	
Coital frequency at last follow-up	≥2 per week	41 (41)	27 (44.3)	14 (35.9)	0.240
	1 per week	36 (36)	18 (29.5)	18 (46.2)	
	1–3 per month	23 (23)	16 (26.2)	7 (17.9)	
	<1 per month	0 (0)	0 (0)	0 (0)	
Females					
Age (years)		31.8 (29.7–34.1)	31.1 (29.2–33.3)	33.1 (30.5–35.0)	0.008*
Education level	Secondary	12 (12)	6 (9.8)	6 (15.4)	0.530
	Tertiary or above	88 (88)	55 (90.2)	33 (84.6)	
Smoking	Never	96 (96)	59 (96.7)	37 (94.9)	0.731
	Quitted	3 (3)	1 (1.6)	2 (5.1)	
	Current	1 (1)	1 (1.6)	0 (0)	
Alcohol	Non-drinker	32 (32)	18 (56.3)	14 (35.9)	0.607
	Social drinker	64 (64)	41 (64.1)	23 (59.0)	
	Drinker	4 (4)	2 (3.3)	2 (5.1)	
BMI (kg/m^2)	<25	92 (92)	56	36 (92.3)	1.000
	≥25 and <30	6 (6)	4	2 (5.1)	
	≥30	2 (2)	1	1 (2.6)	
AMH level (ng/mL)		3.4 (1.8–5.5)	4.0 (2.4–6.0)	3.2 (1.5–3.9)	0.038*
HbA1c (%)		5.2 (5.0–5.4)	5.2 (5.1–5.4)	5.1 (5.0–5.4)	0.725
Total cholesterol (mmol/L)		4.5 (3.9–5.1)	4.3 (3.8–5.1)	4.6 (4.2–5.0)	0.145
Triglycerides (mmol/L)		0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.9 (0.6–1.1)	0.809
HDL-cholesterol (mmol/L)		1.6 (1.4–1.9)	1.6 (1.3–1.8)	1.7 (1.5–1.9)	0.046*
LDL-cholesterol (mmol/L)		2.3 (2.0–2.7)	2.2 (1.9–2.7)	2.4 (2.1–2.9)	0.299
Perceived Stress Scale score		17 (14–19)	17 (14–20)	17 (14–19)	0.766
MET (min/week)		1386 (742–3514)	1533 (792–3072)	1067 (692–3690)	0.496
Males					
Age (years)		33.5 (30.3–35.9)	33.0 (29.3–35.4)	34.5 (31.8–37.2)	0.064
Education level	Secondary	15 (15)	7 (11.5)	8 (20.5)	0.257
	Tertiary or above	85 (85)	54 (88.5)	31 (79.5)	
Smoking	Never	76 (76)	44 (72.1)	32 (82.1)	0.532
	Quitted	14 (14)	10 (16.4)	4 (10.3)	
	Current	10 (10)	7 (11.5)	3 (7.7)	
Alcohol	Non-drinker	15 (15)	10 (16.4)	5 (12.8)	0.942
	Social drinker	74 (74)	44 (72.1)	30 (76.9)	
	Drinker	11 (11)	7 (11.5)	4 (10.3)	
BMI (kg/m^2)	<25	59 (59)	39 (63.9)	20 (51.3)	0.443
	≥25 and <30	34 (34)	18 (29.5)	16 (410)	
	≥30	7 (7)	4 (6.6)	3 (7.7)	
HbA1c (%)		5.4 (5.2–5.5)	5.4 (5.2–5.5)	5.4 (5.1–5.7)	0.756

Continued

Table 1 Continued

Parameter	Overall	Conception within 1 year		P value
		Yes (n=61)	No (n=39)	
Total cholesterol (mmol/L)	4.6 (4.1–5.3)	4.7 (4.3–5.2)	4.5 (4.0–5.7)	0.454
Triglycerides (mmol/L)	1.4 (1.1–2.1)	1.6 (1.2–2.1)	1.3 (1.1–2.1)	0.613
HDL-cholesterol (mmol/L)	1.3 (1.1–1.4)	1.2 (1.1–1.4)	1.3 (1.2–1.5)	0.039*
LDL-cholesterol (mmol/L)	2.7 (2.1–3.2)	2.8 (2.3–3.2)	2.3 (1.9–3.3)	0.165
Sperm concentration (million/mL)	72.6 (36.6–121.8)	84.7 (36.2–144.5)	59.9 (41.8–96.0)	0.054
Sperm progressive motility (%)	45 (38–50)	46 (38–52)	43 (37–48)	0.162
Sperm morphology (%)	4 (3–5)	4 (3–6)	4 (2–5)	0.219
Total motile sperm count (million)	102.5 (49.6–200.4)	128.0 (62.8–245.3)	66.6 (36.4–186.3)	0.030*
TMNC (million)	4.3 (1.6–8.3)	5.1 (1.9–12.0)	2.8 (1.4–5.5)	0.015*
Perceived Stress Scale score	16 (14–19)	16 (14–18)	16 (13–19)	0.977
MET (min/week)	1939 (1059–4119)	1739 (955–3687)	2388 (1386–6360)	0.247

Categorical variables are presented as n (%) while continuous variables are presented as median (25th–75th percentile).
Fisher's exact test and Mann–Whitney U-test were used to compare categorical and continuous variables between groups, respectively.
*Statistically significant.
AMH, anti-Müllerian hormone; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent task; TMNC, total motile normal morphology sperm count.

AMH is a polypeptide hormone solely secreted by granulosa cells of preantral and small antral ovarian follicles in the adult female. Serum AMH level demonstrates negligible fluctuation throughout the menstrual cycle,[3] and hence represents a reliable marker of the ovarian reserve.[4] As ovarian ageing is one important factor leading to reduced fecundability in women, studies have tried to explore the ability of AMH measurement to predict natural fecundability in the general population with contrasting results.[5–10]

Conversely, although semen analysis is a standard investigation for couples presenting with subfertility, and that the fifth edition of the WHO manual (2010) revised the reference range based on a more evidence-based approach,[11] its role in predicting fecundability in the general population still remains poorly defined[12] and it was not adopted in many studies looking into fecundability.[5 8–10]

Besides, the correlation between a number of health and lifestyle factors such as coital frequency, obesity, metabolic problems and physical activity with fecundability is also of interest. Obesity as well as higher non-fasting serum free cholesterol concentrations in both men and women are associated with reduced fecundability.[13–15]

Other lifestyle factors may also impact on fecundability. It was reported that physical activity has an influence on fecundability, in that physical activity of any type might improve fertility among overweight and obese women, whereas lean women who substitute vigorous exercise with moderate exercise may have improved fertility.[16] Perceived stress was also reported to be associated with reduced fecundability in women.[17]

Apparently, fecundability is subject to influence by multiple factors in both the male and the female, and yet most of the existing studies examined individual factors without taking into consideration the partner's factors. We carried out this prospective observational study to investigate the independent effects of age, serum AMH level and semen parameters, when controlled for each other, on fecundability in couples planning for conception. The effect of coital frequency, obesity, metabolic factors, stress level and physical activity were also studied. We hypothesised that these factors have a potential effect on fecundability.

METHODS

Subjects and data collection

This was a prospective observational study with 1 year follow-up. Participants were recruited at the Pre-Pregnancy Check-Up Service of the Family Planning Association of Hong Kong, a primary sexual and reproductive healthcare institution. Recruitment was conducted between November 2015 and April 2017, with the last follow-up completed in March 2019. Study participants were couples who were planning to conceive, had stopped contraception for not more than 6 months or about to stop contraception, and the women were nulliparous and aged between 20 and 44 years. Exclusion criteria included history of infertility, having no sexual exposure or history of coital dysfunction, history of tuboperitoneal disease, pelvic inflammatory disease, ectopic pregnancy or endometriosis, anovulation or irregular menstrual cycles (cycle length <21 or >35 days), known endocrine disease, use of hormonal treatment which might affect ovarian or testicular functions within 3 months, use of injectable

Table 2 Univariate logistic regression analysis of factors predicting conception within 1 year

Coital frequency at last follow-up	Odds ratio (95% CI)	P value
≥2 per week	Reference	0.408
<2 per week	0.71 (0.31 to 1.61)	
Females		
Age (years)	0.83 (0.73 to 0.94)	0.004*
BMI (kg/m^2)	0.99 (0.86 to 1.13)	0.825
AMH level (ng/mL)	1.20 (1.01 to 1.43)	0.038*
HbA1c (%)	0.72 (0.21 to 2.48)	0.599
Total cholesterol (mmol/L)	0.70 (0.40 to 1.21)	0.204
Triglycerides (mmol/L)	0.76 (0.31 to 1.88)	0.551
HDL-cholesterol (mmol/L)	0.30 (0.10 to 0.95)	0.040*
LDL-cholesterol (mmol/L)	0.81 (0.43 to 1.52)	0.503
Perceived Stress Scale score	1.01 (0.92 to 1.11)	0.817
MET (min/week)	1.00 (1.00 to 1.00)	0.515
Males		
Age (years)	0.92 (0.84 to 1.00)	0.055
BMI (kg/m^2)	0.95 (0.84 to 1.07)	0.413
HbA1c (%)	0.69 (0.23 to 2.07)	0.509
Total cholesterol (mmol/L)	1.05 (0.68 to 1.62)	0.835
Triglycerides (mmol/L)	1.18 (0.82 to 1.69)	0.369
HDL-cholesterol (mmol/L)	0.23 (0.05 to 1.13)	0.070
LDL-cholesterol (mmol/L)	1.28 (0.78 to 2.11)	0.323
Total motile sperm count (million)	1.00 (1.00 to 1.01)	0.152
TMNC (million)	1.11 (1.02 to 1.20)	0.016*
Perceived Stress Scale score	1.00 (0.90 to 1.11)	0.954
MET (min/week)	1.00 (1.00 to 1.00)	0.496

*Statistically significant.
AMH, anti-Müllerian hormone; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent task; TMNC, total motile normal morphology sperm count.

hormonal contraception within 6 months, men with azoospermia, and known medical or genetic diseases that the couple had which might affect fertility.

Written informed consent was sought from the participants. The research nurse conducted an interview with each couple to obtain demographic information, and medical and reproductive history using a standardised questionnaire. The English and Chinese versions of the International Physical Activity Questionnaire – Short Form (IPAQ-SF)[18 19] were used to assess physical activity for all participants. Activity was expressed as metabolic equivalent task (MET) minutes per week. Stress level was measured by the Perceived Stress Scale score (PSS-10).[20] Anthropometric measurements of the couple including body height and weight were recorded. The serum AMH level of the women was measured by the Access AMH assay (Beckman-Coulter Inc., Marseille, France).[21] Glycated haemoglobin (HbA1c) and lipid profile were measured for the couple. Semen analysis was done according to the WHO manual (fifth edition). If there was an abnormal parameter(s), another semen analysis was repeated 3 months later. The sample was collected after sexual abstinence for 2–7 days. The mean value was taken if the first one was abnormal and semen analysis was repeated.

Telephone follow-up was conducted at 6 and 12 months after recruitment to obtain information on contraception, coital and pregnancy history. For couples who had regular unprotected intercourse for less than 12 months, telephone follow-up was repeated after trying for 12 months. Couples who did not have regular unprotected intercourse 12 months after recruitment were withdrawn from the study.

Outcome measures

The primary outcome measures were conception at 1 year and time to pregnancy in those who conceived. Conception was defined as a positive urine pregnancy test as reported by patients on telephone follow-up. Time to pregnancy was counted from the time when the couple started to have regular unprotected intercourse without contraception.

Statistics

A minimum sample size of 81 would be adequate to determine a statistical significance between a receiver operating characteristic (ROC) curve with area under the curve of 0.75 and one with the null hypothesis value of 0.5, with power of 80% and type I error of 0.05. Allowing for a dropout rate of 30%, which would be excluded from data analysis, we intended to recruit 120 couples. This would also fulfil the recommended minimum sample size of 100 for estimating the predictive value of individual factors on infertility in a univariate logistic regression model.

Continuous variables, expressed as median (25th–75th percentile), were compared between those who conceived and those who did not after ceasing contraception for 1 year by Mann–Whitney U-test. Fisher's exact test was used to compare categorical variables between groups. Univariate binary logistic regression was used to study the predictive value of those individual parameters on conception at 1 year. Age and serum AMH level of the women, total motile normal morphology sperm count (TMNC) and coital frequency were entered into a standard multivariate binary logistic regression model to study their predictive roles after controlling for each other. ROC curve analysis was applied to determine the predictive value on conception at 1 year. Among those who conceived within 1 year, correlation between clinical parameters and time to pregnancy was determined by Spearman's correlation. Statistical analysis was performed using the IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software version 15 (MedCalc Software bvba, Ostend, Belgium). A

Table 3 Predicting conception within 1 year by multivariate logistic regression analysis where the age and serum anti-Müllerian hormone level of the women and total motile normal morphology count of the men's semen were entered

Parameter	OR (95% CI)	P value
Women's age (years)	0.87 (0.76 to 0.99)	0.032*
Serum AMH level (ng/mL)	1.13 (0.94 to 1.35)	0.189
TMNC (million)	1.09 (1.00 to 1.19)	0.047*

*Statistically significant.
AMH, anti-Müllerian hormone; OR, odds ratio; TMNC, total motile normal morphology sperm count.

two-tailed value of $p<0.05$ was considered statistically significant.

Patient and public involvement

This was solely an investigator-initiated study. There was no patient or public involvement in the design or execution of this study.

RESULTS

A total of 112 couples were recruited, of which 100 completed the study and were eligible for analysis. Among the other 12 couples, five were lost to follow-up, five did not attempt conception by the end of the study period, one divorced and one had assisted reproductive treatment in another clinic before the end-of-study follow-up. For the 100 couples, all women were Chinese, 99 men were Chinese and one man was Caucasian. Two women were using hormonal contraception as their last method of contraception, one was using an intrauterine device, whereas the rest were using barrier or natural contraception. Characteristics of the participants are shown in table 1.

Of the 100 analysed couples, 61 got pregnant within 1 year, with median time to pregnancy of 2 (1–5) months; 39 did not get pregnant in 1 year and fulfilled the definition of infertility. Those who conceived within 1 year, compared with those who did not, had significantly younger age and higher serum AMH level of the women, as well as total motile sperm count and TMNC (table 1).

Couples who conceived within 1 year also had lower HDL-cholesterol in both the female and male partner, although the magnitude of difference was very small. Other clinical parameters including coital frequency, age of men, body mass index (BMI), HbA1c, triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, PSS-10 score and physical activity (MET/week in the IPAQ-SF) of the men and women were not statistically different between the two groups ($p>0.05$). The results are shown in table 1.

Univariate logistic regression of factors predicting conception within 1 year by univariate analysis found that age, AMH and high-density lipoprotein (HDL) cholesterol level of the women, as well as TMNC, were significant factors predicting conception within 1 year (table 2). When the age and serum AMH level of the women, and TMNC were entered for multivariate analysis, the female's age and TMNC, but not serum AMH level of the women, were significant independent factors predicting conception within 1 year (table 3).

Table 4 shows the correlation between time to pregnancy and clinical parameters in the women and men using Spearman's correlation. No parameter was significantly correlated with the time to pregnancy within 1 year. There was no significant difference in time to pregnancy ($p=0.643$) between those having sexual intercourse twice per week or more and less than twice per week. Cox proportional hazards regression analysis revealed that women's age ($p=0.012$), but not serum AMH nor TMNC, significantly contributed to prediction of time to pregnancy (online supplementary table 1). The survival curve showing occurrence of pregnancy with time is shown in online supplementary figure 1.

Table 4 Spearman's correlation between time to pregnancy and the clinical parameters in the participants who conceived in 1 year (n=61)

Parameter	Correlation coefficient	P value
Females		
Age (years)	0.23	0.075
BMI (kg/m^2)	0.15	0.249
AMH level (ng/mL)	−0.12	0.343
HbA1c (%)	−0.20	0.126
Total cholesterol (mmol/L)	0.07	0.572
Triglycerides (mmol/L)	0.02	0.903
HDL-cholesterol (mmol/L)	0.08	0.560
LDL-cholesterol (mmol/L)	0.13	0.316
Perceived Stress Scale	−0.05	0.680
MET (min/week)	0.24	0.091
Males		
Age (years)	0.16	0.217
BMI (kg/m^2)	0.13	0.327
HbA1c (%)	−0.25	0.060
Total cholesterol (mmol/L)	0.08	0.541
Triglycerides (mmol/L)	0.15	0.240
HDL-cholesterol (mmol/L)	−0.06	0.638
LDL-cholesterol (mmol/L)	0.11	0.420
Total motile sperm count (million)	0.01	0.951
TMNC (million)	−0.03	0.808
Perceived Stress Scale score	−0.01	0.920
MET (min/week)	−0.08	0.574

AMH, anti-Müllerian hormone; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent task; TMNC, total motile normal morphology sperm count.

The areas under the ROC curve for women's age and TMNC in semen in predicting conception within 1 year were 0.66 (95% CI 0.55 to 0.77) and 0.65 (95% CI 0.54 to 0.75), respectively, and that of the multivariate logistic regression model combing the two factors was 0.70 (95% CI 0.60 to 0.79).

DISCUSSION

Findings from the present study suggested that the women's age and TMNC, but not serum AMH level, were significant factors predicting conception after trying for 1 year. A previous prospective observational study reported that 82% of couples conceived during 12 cycles.[22] Another prospective study among those practising timed intercourse reported that 89.6% of women conceived in 1 year.[23] However, an internet-based prospective study from Denmark reported a pregnancy rate of 69.6% only at 12 months.[24] In our study, however, only 61% of couples conceived in 1 year. The apparently lower figure could be due to the relatively low coital frequency in our population, even among pregnancy planners. Less than 50% of our cohort had sexual intercourse at least two times per week. In a study of Hong Kong women attending family planning and pre-pregnancy check-up services in 2007–2009, 18.1% had intercourse less than 12 times in a year.[25]

Increasing women's age was demonstrated to be a good predictor of reduced fecundability, while men's age was not associated with fecundability after adjustment for the women's age.[26] In the 501 couples of the Longitudinal Investigation of Fertility and the Environment (LIFE) study, men's age was associated with fecundability.[27] However, the women's age was not controlled for in that study, and it could be that older men merely had older female partners. Our study suggested that older women, but not men, were associated with reduced fecundability. Reproductive ageing in men generally occurs at the more extreme end of the age range.[28] Given that majority of our study participants were in the young range (all men were aged ≤50 years) it is not unexpected that men's age was not observed to have an independent influence on fecundability.

Semen parameters have been reported to be associated with time to pregnancy.[27 29] In line with that, reduced TMNC was found to be significantly associated with reduced fecundability in our study. Obviously, this determines the number of sperms available at the site of fertilisation after the sexual act. However, this is not the sole determinant as other factors such as coital frequency would be important also.

It is worthwhile to note that fecundability is subjected to multifactorial influence. The predictive value of either the women's age or TMNC alone or in combination was just modest, as shown by the c-statistics in the ROC curves, despite the statistical significance of the individual factors.

Steiner *et al* reported that AMH was associated with day-specific probability of pregnancy.[5] A study of 750 women from the same group found that low AMH was not associated with reduced fecundability.[9] Other studies involving younger healthy pregnancy planners found that AMH did not predict natural fertility.[6 7 10] An observational study of 87 women who had a live birth from planned natural pregnancy found that AMH was not related to the time to pregnancy.[8] The women in our study were younger (only 17% were aged 35+ years) and our results concurred with those studies involving younger women.

Cholesterol is a substrate for steroidogenesis and hence may impact on fertility .[30] The LIFE study found that higher free cholesterol was associated with reduced fecundability independent of BMI.[15] A secondary analysis in the Effects of Aspirin in Gestation and Reproduction trial in 2017 also found that reduced fecundability was associated with all lipoprotein abnormalities including low HDL-cholesterol.[31] Our results revealed that lower HDL-cholesterol was significantly associated with conception at 1 year; however, the magnitude of difference was extremely small, and is unlikely to be clinically meaningful. We also studied the effect of HbA1c, a glycaemic index, on fecundability, which has not been reported in the literature. No significant effect of HbA1c on fecundability was suggested in our cohort. This could be limited by the fact that no one in our cohort had abnormal HbA1c at or above 6.0%.

A previous study reported that a total MET of 1200–1740 min/week was associated with highest fecunability.[16] Although couples who conceived in 1 year in our cohort had similar MET results, we could not demonstrate a significant effect of physical activity on fecundability, probably because the majority of the individuals in our cohort were not doing vigorous physical activity.

The main strength of our study is that it was a prospective study with 1 year follow-up and both the male and female partners of the couples were closely followed up so as to avoid recall bias. The subjects were recruited among pregnancy planners in the community, in contrast to some previous studies which targeted couples attending infertility clinics. However, our sample size was only modest, and it was just adequate to confer adequate power for our main analyses. A larger further study with adequate power to establish and validate a prediction model by the women's age and TMNC would be worthwhile. Another limitation was that semen parameters and lifestyle factors such as smoking, exercise and stress level may fluctuate or change with time. We only assessed these parameters at recruitment, which may not represent the whole course of the follow-up period. The fact that the majority of the couples were non-smokers and had normal BMIs may make the comparison of these parameters difficult and limit its predicting power, and our findings cannot be extrapolated to couples with more extreme BMIs.

CONCLUSIONS

In conclusion, women's age and TMNC are significant independent predictors of conception within 1 year. No parameter can predict the time to pregnancy within 1 year. This finding can aid preconceptional counselling of couples who are ceasing contraception in preparation for pregnancy.

Acknowledgements The authors would like to thank Ms Celia Ng and Ms Wylie Wong for co-ordinating subject recruitment and follow-up. They also want to express their gratitude to all staff members of the Family Planning Association of Hong Kong who facilitated the conduct of this study, and to Ms Benency Po-Chau Wong and Dr Angel Chan for performing the biochemical assays. Lastly, they thank all the couples who participated in this study.

Contributors HWRL, WSBY, PCHO and EHYN conceived and designed the study. MTL, HWRL, GCYW and EHYN supervised subject recruitment and follow-up. MTL analysed the data, interpreted the results and drafted the manuscript. All authors provided critical revisions and approved the final manuscript prior to submission.

Funding This study was supported by internal research funding from the Department of Obstetrics and Gynaecology, The University of Hong Kong.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethics approval was obtained from both the Institutional Review Board of the University of Hong Kong and the Hospital Authority Hong Kong West Cluster. Approval was also obtained from the Health Services Subcommittee, Family Planning Association of Hong Kong.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Mei Ting Lam http://orcid.org/0000-0003-4882-5151
Hang Wun Raymond Li http://orcid.org/0000-0002-7957-7798

REFERENCES

1 Zegers-Hochschild F, Adamson GD, Dyer S, *et al*. The international glossary on infertility and fertility care, 2017. *Hum Reprod* 2017;32:1786–801.
2 Sobotka T. Is lowest-low fertility in Europe explained by the postponement of childbearing? *Popul Dev Rev* 2004;30:195–220.
3 La Marca A, Stabile G, Artenisio AC, *et al*. Serum anti-Mullerian hormone throughout the human menstrual cycle. *Hum Reprod* 2006;21:3103–7.
4 Iliodromiti S, Kelsey TW, Wu O, *et al*. The predictive accuracy of anti-Müllerian hormone for live birth after assisted conception: a systematic review and meta-analysis of the literature. *Hum Reprod Update* 2014;20:560–70.
5 Steiner AZ, Herring AH, Kesner JS, *et al*. Antimüllerian hormone as a predictor of natural fecundability in women aged 30-42 years. *Obstet Gynecol* 2011;117:798–804.
6 Hagen CP, Vestergaard S, Juul A, *et al*. Low concentration of circulating antimüllerian hormone is not predictive of reduced fecundability in young healthy women: a prospective cohort study. *Fertil Steril* 2012;98:1602–8.
7 Depmann M, Broer SL, Eijkemans MJC, *et al*. Anti-Müllerian hormone does not predict time to pregnancy: results of a prospective cohort study. *Gynecol Endocrinol* 2017;33:644–8.
8 Streuli I, de Mouzon J, Paccolat C, *et al*. AMH concentration is not related to effective time to pregnancy in women who conceive naturally. *Reprod Biomed Online* 2014;28:216–24.
9 Steiner AZ, Pritchard D, Stanczyk FZ, *et al*. Association between biomarkers of ovarian reserve and infertility among older women of reproductive age. *JAMA* 2017;318:1367–76.
10 Korsholm A-S, Petersen KB, Bentzen JG, *et al*. Investigation of anti-Müllerian hormone concentrations in relation to natural conception rate and time to pregnancy. *Reprod Biomed Online* 2018;36:568–75.
11 World Health Organization. *WHO laboratory manual for the examination and processing of human semen*. 5th edn. Geneva: WHO Press, 2010.
12 Esteves SC, Zini A, Aziz N, *et al*. Critical appraisal of World Health Organization's new reference values for human semen characteristics and effect on diagnosis and treatment of subfertile men. *Urology* 2012;79:16–22.
13 Gesink Law DC, Maclehose RF, Longnecker MP, *et al*. Obesity and time to pregnancy. *Hum Reprod* 2007;22:414–20.
14 Ramlau-Hansen CH, Thulstrup AM, Nohr EA, *et al*. Subfecundity in overweight and obese couples. *Hum Reprod* 2007;22:1634–7.
15 Schisterman EF, Mumford SL, Browne RW, *et al*. Lipid concentrations and couple fecundity: the life study. *J Clin Endocrinol Metab* 2014;99:2786–94.
16 Wise LA, Rothman KJ, Mikkelsen EM, *et al*. A prospective cohort study of physical activity and time to pregnancy. *Fertil Steril* 2012;97:1136–42.
17 Wesselink AK, Hatch EE, Rothman KJ, *et al*. Perceived stress and fecundability: a preconception cohort study of North American couples. *Am J Epidemiol* 2018;187:2662–71.
18 Craig CL, Marshall AL, Sjöström M, *et al*. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;35:1381–95.
19 Macfarlane DJ, Lee CCY, Ho EYK, *et al*. Reliability and validity of the Chinese version of IPAQ (short, last 7 days). *J Sci Med Sport* 2007;10:45–51.
20 Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapam S, Oskamp S, eds. *The social psychology of health: Claremont Symposium on applied social psychology*. Newbury Park (CA: SAGE, 1988.
21 Li HWR, Wong BPC, Ip WK, *et al*. Comparative evaluation of three new commercial immunoassays for anti-Müllerian hormone measurement. *Hum Reprod* 2016;31:2796–802.
22 Zinaman MJ, Clegg ED, Brown CC, *et al*. Estimates of human fertility and pregnancy loss. *Fertil Steril* 1996;65:503–9.
23 Gnoth C, Godehardt D, Godehardt E, *et al*. Time to pregnancy: results of the German prospective study and impact on the management of infertility. *Hum Reprod* 2003;18:1959–66.
24 Wise LA, Rothman KJ, Mikkelsen EM, *et al*. An internet-based prospective study of body size and time-to-pregnancy. *Hum Reprod* 2010;25:253–64.
25 Lo SS-T, Kok W-M. Sexual behavior and symptoms among reproductive age Chinese women in Hong Kong. *J Sex Med* 2014;11:1749–56.

26 Wesselink AK, Rothman KJ, Hatch EE, *et al*. Age and fecundability in a North American preconception cohort study. *Am J Obstet Gynecol* 2017;217:667.e1–667.e8.

27 Buck Louis GM, Sundaram R, Schisterman EF, *et al*. Semen quality and time to pregnancy: the Longitudinal Investigation of Fertility and the Environment study. *Fertil Steril* 2014;101:453–62.

28 Lai SF, Li RH, Yeung WS, *et al*. Effect of paternal age on semen parameters and live birth rate of in-vitro fertilisation treatment: a retrospective analysis. *Hong Kong Med J* 2018;24:444–50.

29 Bonde JP, Ernst E, Jensen TK, *et al*. Relation between semen quality and fertility: a population-based study of 430 first-pregnancy planners. *Lancet* 1998;352:1172–7.

30 DeAngelis AM, Roy-O'Reilly M, Rodriguez A, *et al*. Genetic alterations affecting cholesterol metabolism and human fertility. *Biol Reprod* 2014;91:1–10.

31 Pugh SJ, Schisterman EF, Browne RW, *et al*. Preconception maternal lipoprotein levels in relation to fecundability. *Hum Reprod* 2017;32:1055–63.