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Birth characteristics in a clinical sample of women seeking infertility treatment: a case–control study

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ABSTRACT

Objective: To determine the distribution of low birth weight (LBW), preterm birth, small for gestational age (SGA) and large for gestational age (LGA) by main cause of infertility (female, combined, male, unexplained) in women seeking infertility treatment.

Design: A case–control study.

Setting: A Centre for Reproductive Medicine in Sweden.

Participants: All women (n=1293) born in Sweden in 1973 or later and who were part of heterosexual couples seeking infertility treatment at a Centre of Reproductive Medicine from 2005 to 2010 were asked to participate. Those who had not begun the diagnostic process and who declined participation in the study were excluded. In total, 1206 women (94.5%) participated in the study.

Main outcome measures: Main cause of infertility (female, combined, male, unexplained) collected from the patients' medical charts. LBW (<2500 g), preterm birth (<37 weeks), SGA (<−2SD of the mean weight for the gestational length) and LGA (>+2SD of the mean weight for the gestational length), collected from the Swedish Medical Birth Register.

Results: The risk of being born with LBW was increased about 2.4 times (OR=2.40, CI 1.13 to 5.07, p=0.02) in women seeking treatment for infertility due to female causes rather than for male or unexplained causes. Women with a female infertility factor were 2.7 times more likely to be born SGA (OR=2.73, CI 1.02 to 7.34, p=0.047) compared with those in whom the cause of infertility was unexplained.

Conclusions: Women born with LBW or SGA seem to suffer an increased risk of infertility due to a female factor. Thus, infants born with birth characteristics that deviate from the norm may be at greater risk of difficulties in childbearing later on in life. Since this study is the first of its kind, more studies are needed to verify the associations found in this study and to determine their nature.

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Strengths and limitations of this study

- No previous studies have examined the possible association between birth characteristics and infertility later on in life.
- The results suggest that women born with low birth weight and/or small for gestational age are at increased risk of infertility later on in life.
- This study is based on data from the national Medical Birth Register, which is a reliable source of data decreasing dependence on unsecure patient data.
- Women diagnosed with infertility were compared with those who had a spouse with a male infertility factor or the women where the cause of infertility was unexplained since a well-matched control group would be difficult to form.

care, survival is the expected outcome for these individuals. However, there may be health implications of being born prematurely or with LBW. Studies have shown an association between restricted fetal growth and diseases later in life, for example those inherent to the metabolic syndrome.[1–4] One theory giving a plausible explanation of this connection is Barker's 'the foetal origins of adult disease hypothesis'.[2 5] This hypothesis states that when the fetus is exposed to an unfavourable environment, the development of body systems will be affected, resulting in a change in their function. These changes become risk factors for disease later in life.[2 5] Previous studies have shown some variations from the norm regarding the function and structure of the reproductive organs as well as the reproductive patterns among individuals born with VLBW (meaning <1500 g), or small for gestational age (SGA; meaning a birth weight <−2SD of the mean weight for the gestational length).[6–8] One Swedish study showed that women born with VLBW were less likely, whereas women born SGA were more likely, to give birth during their early reproductive years compared with controls.[9–12] Studies have indicated that there

INTRODUCTION

Only a few decades ago, mortality was high in infants born very prematurely and/or with very low birth weight (VLBW). Nowadays, owing to advances in medical research and

may be abnormalities in hormonal levels and testes size in adult men born growth restricted while, in women, reduced ovulation rate and smaller internal genitalia were found.[13–15]

There are thus studies indicating that there may be abnormalities in the function and structure of the reproductive organs as well as reproductive patterns in individuals born small, growth restricted and/or prematurely. However, there are no previous studies on the possible association between birth characteristics and infertility among these individuals.

The aim of the present study was to examine the distribution of LBW, SGA, LGA (large for gestational age) and premature birth in a population of Swedish women, each being part of a couple seeking treatment for infertility due to female causes rather than male or unexplained causes.

We hypothesised that the functions of the reproductive system are affected by growth restriction and/or premature birth, as stated by Barker's hypothesis, which will manifest itself as an increased number of individuals born prematurely, SGA or with LBW in women seeking treatment for infertility due to female causes rather than male or unexplained causes.

METHODS
Population
This was a retrospective case–control register study, which included all women born in Sweden in 1973 or later who were part of a heterosexual couple accepted for infertility treatment at the Centre for Reproductive Medicine (RMC), Linköping University Hospital, Sweden, from 1 January 2005 to 31 December 2010. This time period was selected to include a maximum number of women seeking infertility treatment who were included in the national Medical Birth Register (MBR), which was created in 1973. Those who had neither filled out the introductory health questionnaire nor had laboratory tests taken, and thus had not undergone a complete diagnostic process, were not included. The remaining 1293 women received a letter asking for the women's permission to access information from their medical charts and the MBR. Permission was received from 94.5% (n=1222) of the women. Throughout this article, the woman is the unit of analysis, and in all instances that birth characteristics are described, it is the woman's own birth characteristics that are referred to and in no case her offspring.

Infertility treatment at RMC, Linköping University hospital
Couples who are infertile and who are living in the southeast healthcare region of Sweden, which has a population of 1.7 million inhabitants, can receive a referral to RMC, Linköping University hospital for infertility treatment. In order to be accepted for the treatment paid by the County Council of Östergötland, responsible for healthcare in the region, a number of

criteria stated in the department's guidelines must be fulfilled, including an upper body mass index (BMI) limit of 30 kg/m^2 for the woman. Also, the couple must be married or cohabiting for at least 2 years before they are accepted for treatment.

Couples accepted for infertility treatment are routinely asked to fill out a questionnaire which contains questions regarding age, height and weight, chronic illnesses, smoking (1, yes; 2, no), the use of snuff (1, yes; 2, no), regular intake of medication and allergies. Also, information about the number of previous pregnancies, children, abortions and miscarriages is requested. This information is added to the patients' medical charts. After that, an individually adapted investigation of the cause of infertility is performed. This investigation includes sperm samples, gynaecological examination and an ultrasound including diagnosis of patent fallopian tubes, laboratory tests etc. Information about the type of infertility treatment chosen is noted in the patient's medical charts.

Information gathered from medical charts
For the present study, information was collected from the medical charts of the participants about the information given in the introductory questionnaire and also about infertility type (1, female; 2, male; 3, combined; 4, unexplained), which had been determined by the physician conducting the infertility investigation. The information was retrieved from the patients' charts by two midwives trained in assisted reproduction and by the corresponding author. Patients were asked to state any chronic illnesses in an open-ended question which, for this study, was grouped into relevant categories by the corresponding author. BMI was calculated from the height and weight and divided into four categories (1, <18.5 kg/m^2; 2, 18.5–24.99 kg/m^2; 3, 25.00–29.99 kg/m^2; 4, ≥30.00 kg/m^2).[16]

The national Medical Birth Register
Information regarding the birth characteristics of the women was collected from the national MBR, which includes information on 97–99% of pregnancies that have resulted in deliveries in Sweden since 1973. The register contains information about the pregnancy, delivery and antenatal health of the child and is based on the medical charts from maternal healthcare, obstetric care and infant care.[8] The MBR is thoroughly described by Harlow et al.[17] The information collected about the birth characteristics of the woman included the height, weight and birth week. Those weighing ≤2500 g were classified as being LBW, those weighing ≤1500 were classified as being VLBW and those whose birth weight was smaller than −2SD of the mean weight for the gestational length were classified as being SGA, while those larger than +2SD of the mean weight for the gestational length were classified as LGA.[17 18] Moderate preterm birth was defined as being born before gestational week

37 while very preterm birth was defined as being born before the 32nd week.[6]

Statistics

Statistical analyses were performed using IBM SPSS V.20 (IBM Inc, Armonk, New York, USA). All analyses were two-sided and the significance level was set at $p \leq 0.05$. The distributions of year of birth, BMI, highest level of education, LBW, VLBW, LGA, SGA, moderate preterm birth and very preterm birth divided by the number of individuals in the categories female, male, combined and unexplained infertility were calculated. The female and combined categories were added together to form a separate category in order to include all women diagnosed with infertility in the same category. The distribution of the above-mentioned variables was also calculated for this category. For all variables, numbers and percentages were given.

Multinominal regression analyses were performed to determine any differences between the three categories of women; those where the main cause of infertility was female/combined, male or unexplained in regard to preterm birth (<37 weeks), LBW (<2500 g), SGA or LGA. A second set of analyses was performed which included BMI and parity as factors in order to minimise the risk of bias. Bivariate logistic regression was used to determine any differences between the two categories of women: those where the main cause of infertility was female/combined with those where the cause was male/unexplained infertility in regard to preterm birth (<37 weeks), LBW (<2500 g), SGA or LGA. These analyses were also repeated while controlling for BMI and parity. For the regression analyses, VLBW and very preterm birth were not included due to the too small number of positive outcomes in these categories.

RESULTS

A total of 1293 women met the inclusion criteria and thus received a letter of permission. In total, 1222 women (94.5%) agreed to participate in the study. As infertility type was not specified in their medical charts, 16 women were excluded from the analyses. Thus, the population used for statistical analyses consisted of 1206 women (93.3%). Since there was some information lacking in the medical charts, the numbers of participants do not add up to 1206 for all variables. The women were born in 1973–1987 with a median birth year of 1976 (table 1). The infertility was due to female causes in 38.5% (n=464) of the cases, male causes in 26.8% (n=323) of the cases, combined causes in 6.6% (n=79) of the cases and in 28.2% (n=340) of the cases was unexplained. Approximately 69% (n=796) of the women had a normal BMI (18.5–24.99), while 23.2% (n=268) were overweight (25–29.99), 5.2% (n=60) obese (≥30) and 2.4% (n=27) underweight (<18.5; table 1). The corresponding numbers for the category containing the women where the infertility was female or combined

were 66% (n=343), 23.7% (n=123), 7.9% (n=41) and 2.5% (n=13). Hence, there was a tendency for women with a mainly female cause of infertility to be heavier than the average weight for the whole group. About 7.7% of the women (n=90) were smokers while 1.6% (n=19) used snuff regularly (table 1). In regard to previous pregnancies, 22.3% (n=263) had been pregnant previously. The corresponding numbers for women where the infertility was female or combined were 24.2% (n=129). The infertility was primary in 91.4% (1072) of the women, meaning that they had no previous children. Among the women diagnosed with female infertility 10% (n=45) had one or more child. Twelve per cent (n=141) of the women had experienced miscarriages previously. The corresponding numbers for women with a female or combined cause of infertility were 14.2% (n=76), which was higher than for the other groups (table 1).

In regard to self-reported chronic illnesses, 356 (29.5%) of the women reported one or more illness, which corresponded to 278 (60.0%) of the women with a female cause of infertility, 65 (20.1%) with a male cause of infertility, 29 (20.1%) of those where the cause was combined and 84 (24.7%) of those where the cause of infertility was unexplained. The remaining women either did not answer the question or stated that they had no chronic illnesses. The types of illnesses reported are displayed in table 2. When gynaecological conditions were removed, the majority of which consisted of endometriosis, 21.3% of the women with a female cause of infertility stated that they had a chronic illness.

Thirty-three (3.3%) of the women had been born before 37 gestational weeks while 0.4% (n=4) had been born before 32 weeks (table 3). The corresponding numbers for women diagnosed with mainly a female cause of infertility were 3.6% (n=16) and 0.7% (n=3), respectively. Thirty-seven women (3.6%) weighed less than 2500 g at birth, of which 23 belonged to the female or combined infertility category. Only two (0.2%) women had weighed less than 1500 g at birth; both of these belonged to either the female infertility category or the combined infertility category. Forty women (3.3%) had been born SGA while 30 (2.5%) women were born LGA (table 3).

The multinomial regression analyses showed no differences between the three categories (female/combined, male, unexplained) of women in regard to being born prematurely, LBW or LGA (table 4). However, those with a female or combined infertility were 2.5 times more likely to be born SGA than those with an unexplained cause of infertility (OR=2.57, CI 1.04 to 6.36, p=0.041). This difference remained when BMI and parity were controlled for (OR=2.73, CI 1.02 to 7.34, p=0.047). The bivariate regression analyses showed no difference as to being born preterm (<37 weeks), SGA and LGA when women with female or combined causes of infertility were compared with those with a male or unexplained infertility factor. Women with a female or combined

Table 1 Demographics and characteristics of previous pregnancies by infertility type

Birth year*	Female 1977 (1973–1985)		Male 1976 (1973–1987)		Combined 1975 (1973–1983)		Unknown 1976 (1973–1984)		Total 1976 (1973–1984)		Female +Combined 1976 (1973–1985)	
	n	Per cent	n	Per cent	n	Per cent	n	Per cent	n	Per cent	n	Per cent
BMI												
<20	61	13.8	36	11.5	8	10.3	35	10.9	140	12.1	69	13.3
20–24, 99	248	56.1	181	58.0	39	50.0	217	67.6	685	59.4	287	55.2
25–29, 99	102	23.1	80	25.6	21	26.9	65	20.2	268	23.2	123	23.7
>30	31	7.0	15	4.8	10	12.8	4	1.2	60	5.2	41	7.9
Tobacco use												
Smoking												
Yes	32	7.1	30	9.4	8	10.4	20	93.9	90	7.7	40	7.6
No	420	92.9	290	90.6	69	89.6	307	6.1	1086	92.3	489	92.4
Snuff												
Yes	3	99.3	5	1.6	2	2.7	9	2.8	19	1.6	5	1.0
No	447	0.7	313	98.4	73	97.3	319	97.2	1151	98.4	520	99.0
Number of previous pregnancies												
0	344	75.4	260	81.5	60	77.9	254	77.2	918	77.7	404	75.8
1–2	101	22.1	55	17.2	14	18.2	64	19.5	234	19.8	115	21.6
≥3	11	2.4	4	1.3	3	3.9	11	3.3	29	2.5	14	2.6
Number of previous miscarriages												
0	391	85.7	293	91.8	66	85.7	290	88.1	1040	88.1	457	85.7
1–2	58	12.7	26	8.2	11	14.3	32	9.7	127	10.8	69	12.9
≥3	7	1.5	0	0.0	0	0.0	7	2.1	14	1.2	7	1.3
Number of previous abortions												
0	429	94.3	297	93.1	73	96.1	299	90.9	1098	93.1	502	94.5
1	23	5.1	20	6.3	3	3.9	25	7.6	71	6.0	26	4.9
≥2	3	0.7	2	0.6	0	0.0	5	1.5	10	0.8	3	0.6
Number of children												
No children	407	90.0	293	92.1	68	89.5	304	93.0	1072	91.4	475	90.0
≥1 child	45	10.0	25	7.9	8	10.5	23	7.0	101	8.6	53	10.0

*Displayed in median and range.
BMI, body mass index.

Table 2 Prevalence of self-reported chronic illness by type of infertility

	Female		Male		Combined		Unexplained		Total	
	n 464	Per cent 100	n 323	Per cent 100	n 79	Per cent 100	n 340	Per cent 100	n 1206	Per cent 100
Chronic illness										
Dermatological	4	0.9	0	0.0	1	1.3	2	5.9	7	0.6
Congenital malformations or chromosomal abnormalities	5	1.1	1	0.3	1	1.3		5.9	9	0.7
Pulmonary	22	4.7	12	3.7	3	3.8	15	4.4	52	4.3
Asthma	20		12		2		15		49	
Other	2		0		1		0		3	
Gastrointestinal	13	2.8	3	0.9	2	2.6	14	4.1	32	2.7
Inflammatory bowel disease	6		1		1		7		15	
Irritable bowel syndrome	1		0		1		5		7	
Coeliac disease	4		0		0		1		5	
Other	2		2		0		1		5	
Psychiatric	13	2.8	9	2.8	2	2.6	6	1.8	31	2.6
Depression	11	6	1	3	21					
Other	3	3	1	3	10					
Endocrinological	22	4.7	14	4.3	10	7.9	18	5.3	64	5.3
Hypothyroidism	12		6		4		12		34	
Other thyroid disease	2		0		1		2		5	
Diabetes	2		6		2		3		13	
Obesitas	2		1		1		0		4	
Hypertension	2		1		1		0		4	
Hyperprolactinaemia	2		0		1		1		4	
Gynaecological	79	17.0	2	0.6	8	10.1	3	0.9	92	7.6
Endometriosis	76		2*		8		3*		89	
Other	3		0		0		0		3	
Neurological	8	1.7	6	1.9	1	1.3	6	1.8	21	1.7
Multiple sclerosis	2		1		0		1		4	
Epilepsy	4		2		0		0		6	
Migraine	2		2		1		5		10	
Other	0		1		0		0		1	
Rheumatological disease	2	0.4	1	0.3	1	1.3	7	2.1	11	0.9
Fibromyalgia	1	0.2	2	0.6	0	0.0	1	0.3	4	0.3
Muscle and joint dysfunctions	5	1.1	4	1.2	1	1.3	2	0.6	12	1.0
Other symptom, disorder or previous operations	6	1.3	7	2.2	2	2.6	10	3.4	25	2.1

*The responsible physician either did not confirm the diagnosis or did not believe it to be a contributing factor to the infertility.

cause of infertility were about twice as likely to be born with LBW (<2500 g) compared with those with a male or unexplained infertility (OR=2.26, CI 1.13 to 4.52, p=0.021). The differences remained when BMI and parity were controlled for (OR=2.40, CI 1.13 to 5.07, p=0.022; table 4).

DISCUSSION

The present study aimed to investigate the distribution of preterm birth, LBW, SGA and LGA in a population of Swedish women seeking infertility treatment and to compare those where the cause of infertility was female with those where the infertility was male and/or unexplained. The results of the study showed no differences in the distribution of preterm birth or LGA between the categories of women. However, women seeking infertility treatment due to a female factor were about twice as likely to have been born with LBW compared with those where the cause of infertility was male or unexplained, while those with a female factor were about twice as likely to be born SGA compared with those where the infertility factor was unexplained. The bivariate logistic regression analysis showed that the risk of being born with LBW was twice as high among women with a female infertility factor compared with those where the cause of the infertility was male or unexplained. This difference remained when parity and BMI were controlled for. Thus, this study found an association between being born with LBW and subsequent infertility in women, results which are in accordance with our hypothesis. Also, the multinomial regression analyses showed that the risk of being born SGA was increased 2.5 times in women where the cause

Table 3 Birth characteristics by infertility type

Infertility type	Female n 464	Per cent 38.5	Male n 323	Per cent 26.7	Combined n 79	Per cent 6.6	Unexplained n 340	Per cent 28.2	Total n 1206	Per cent 100	Female +Combined n 543	Per cent 45.1
Preterm birth (weeks)												
Moderate (<37)												
Yes	13	3.4	6	2.3	3	4.6	10	3.4	33	3.3	16	3.6
No	368	96.6	256	97.7	62	95.4	283	96.6	980	96.7	430	96.4
Very (<32)												
Yes	3	0.8	0	0.0	0	0.0	1	0.3	4	0.4	3	0.7
No	378	99.2	262	100	65	100	292	99.7	1009	99.6	443	99.3
Birth weight												
LBW (<2500 g)												
Yes	17	4.5	6	2.3	6	9.2	7	2.4	37	3.6	23	5.1
No	365	95.5	256	97.7	59	90.8	286	97.6	978	96.4	424	94.9
VLBW (<1500 g)												
Yes	1	0.3	0	0.0	1	1.5	0	0.0	2	0.2	2	0.4
No	381	99.7	262	100	64	98.5	293	100	1013	99.8	445	99.6
Size in relation to mean weight for gestational age												
SGA (<−2SD)												
Yes	17	3.7	10	3.1	7	8.9	6	1.8	40	3.3	24	4.4
No	447	96.3	312	96.9	72	91.1	334	98.2	1181	96.7	519	95.6
LGA (>2SD)												
Yes	12	2.6	9	2.8	0	0.0	9	2.6	30	2.5	12	2.2
No	452	97.4	313	97.2	79	100	331	97.4	1191	97.5	531	97.8

LBW, low birth weight; LGA, large for gestational age; SGA, small for gestational age; VLBW, very low birth weight.

of infertility was female compared with those where the cause was unexplained. Interestingly, this study also showed that women with a female or combined infertility were more likely to be obese compared with women of the other infertility categories. The obesity could of course be the cause of infertility in these women. However, in accepting these women, exceptions from the clinic guidelines were made. Thus, it is more likely that the cause of infertility was well defined in these women and that the obesity therefore was not considered important. As many as 22.3% (n=263) of all women had been pregnant previously and 8.6% (n=101) had children. A higher percentage of those with a female cause of infertility had previously experienced a miscarriage compared with women in the other groups.

It appears that there is an association between being born with LBW and being diagnosed with infertility later on in life. While there are no previous studies on this topic, Ekholm et al[9] found that women born with VLBW were less likely to give birth during their early reproductive years. We were not able to include VLBW in our analyses due to the too small numbers, but if there is an over-representation of women born with LBW among those diagnosed with infertility, it seems likely that weighing even less at birth should also increase the risk of female infertility. Perhaps the results of Ekholm et al[9] were an early manifestation of an increased risk of infertility in these women.

So what could be the reason for these associations? Could it be that growth restriction influences the function of the reproductive organs resulting in reproductive impairment later on in life? Growth restriction has been linked to smaller internal genitalia and reduced ovulation rate in women,[14 15] results which could be associated with those of the present study.

This study has several limitations. First of all, the sample size was relatively small, which negatively influences the validity of the results. Also, the women diagnosed with infertility were compared with those who were not infertile themselves but who had a spouse with a male infertility factor or the women where the cause of infertility within the couple was unexplained. The category with an unexplained cause of infertility causes difficulties in interpreting the results since it may contain individuals where the cause of infertility was yet to be discovered. It is also possible that the causes of the couples' inability to have children are due to other reasons than infertility such as sexual dysfunction and that not all couples are truthful in reporting the length of time that they have tried to conceive and thus are fertile or subfertile rather than infertile. A strength of this study is the that it is based on robust data from the MBR, decreasing dependence on unsecure patient data on, for example, birth weights, which could include recall bias. However, all registers may also contain errors, but these limitations should affect all groups equally. Another strength is that the infertility diagnoses were

Table 4 Birth characteristics by infertility type: OR

	Multinomial regression, controls			Multinomial regression, no controls			Binary logistic regression, controls			Binary logistic regression, no controls		
	p Value	OR	CI	p Value	OR	CI	p Value	OR	CI	P Value	OR	CI
Variables by infertility type												
Preterm (<37 weeks)												
Female/combined (ref) Male	0.291	1.685	0.639 to 4.441	0.341	1.588	0.613 to 4.109	–	–	–	–	–	–
Female/combined (ref) Unexplained	0.597	1.268	0.525 to 3.063	0.900	1.053	0.471 to 2.353	–	–	–	–	–	–
Female/combined (ref) Male/unexplained	–	–	–	–	–	–	0.332	1.446	0.686 to 3.048	0.530	1.253	0.620 to 2.535
LBW (<2500 g)												
Female/combined (ref) Male	0.095	2.200	0.780 to 2.310	0.071	2.314	0.930 to 5.760	–	–	–	–	–	–
Female/combined (ref) Unexplained	0.057	2.637	0.973 to 7.150	0.069	2.216	0.939 to 5.234	–	–	–	–	–	–
Female/combined (ref) Male/Unexplained	–	–	–	–	–	–	0.022*	2.397	1.134 to 5.065	0.021*	2.262	1.132 to 4.756
LGA												
Female/combined (ref) Male	0.595	0.788	0.327 to 1.900	0.590	0.786	0.327 to 1.886	–	–	–	–	–	–
Female/combined (ref) Unexplained	0.712	0.841	0.335 to 2.108	0.679	0.831	0.346 to 1.994	–	–	–	–	–	–
Female/combined (ref) Male/unexplained	–	–	–	–	–	–	0.591	0.813	0.381 to 1.732	0.573	0.809	0.386 to 1.694
SGA												
Female/combined (ref) Male	0.341	1.469	0.666 to 3.240	0.339	1.443	0.681 to 3.057	–	–	–	–	–	–
Female/combined (ref) Unexplained	0.047*	2.729	1.015 to 7.338	0.041*	2.574	1.041 to 6.364	–	–	–	–	–	–
Female/combined (ref) Male/unexplained	–	–	–	–	–	–	0.064	1.912	0.962 to 3.800	0.057	1.867	0.981 to 3.552

*Significant at the p=0.05 level.
LBW, low birth weight; LGA, large for gestational age; SGA, small for gestational age.

determined by the physicians conducting the infertility investigations, thus being independent from the contributors to the study. Since only Swedish women were included, the results of this study cannot be generalised to include all women as the causes of infertility differ in developing countries from the western world. In future studies, we will describe the type of treatment and treatment outcome in the present study population and also the birth characteristics of their male partners.

In conclusion, this study indicates that there is an association between being born with LBW and/or SGA and infertility in women. As medical research and care advances, more infants will be born and survive with LBW and/or SGA, which in turn might influence future need of infertility treatment. The present study is the first on this topic; thus, more studies are needed to verify these possible associations and to determine their nature.

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