Original Article

Observational Study of the Social Determinants of Health in Subfertile versus Nonsubfertile Women

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Abstract

Context: Subfertility affects about 15% of couples worldwide. There are several factors that affect subfertility called social determinants of health (SDH): biological factors as age, ethnic origin, and body mass index; behavioral factors as alcohol intake, smoking, coffee, dietary restriction, physical activity, and psychological state; and contextual factors as education, work activity, and income level. **Aims:** The aim of the study is to evaluate the distribution's relevance of the SDH in subfertile women versus nonsubfertile women. **Settings and Design:** A prospective comparative study with two groups of women recruited over 1 year at hospital consultation: one group with subfertile women excluding women without a male partner or with a previous child and another one formed by primigravidae, excluding those receiving assisted reproduction techniques to become pregnant. **Subjects and Methods:** We compare the different factors between subfertile and nonsubfertile women one by one. Second, a multivariate analysis was conducted with logistic regression. In all cases, informed consent was obtained. **Results:** Regular physical exercise 3–4 times/week (odds ratio [OR]: 0.33, 95% confidence interval [CI]: 0.15–0.71) or healthy food products such as fish 1–2 times/week (OR: 0.40, 95% CI: 0.17–0.95) were associated with nonsubfertile women. **Conclusions:** The distribution of SDH in natural fertility is not altogether homogeneous. Weight control by means of restricting calorie intake, greater consumption of healthy foods such as fish, regular physical exercise, and lower age are positively associated with fertility. Population-level intervention is possible to improve women's health, as these are modifiable factors. Ethnic origin can be considered as a relevant factor, as it may condition the distribution of other determinants.

Keywords: *Body weight, exercise, fertility, lifestyle, smoking, social determinants of health*

Introduction

Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" (World Health Organization [WHO] definition). Problems related to fertility or subfertility affect around 15% of couples of reproductive age worldwide,[1] which represents a prevalence of approximately 9%.[2] Subfertility, understood as a difficulty but not impossibility to conceive, generates economic and biopsychosocial consequences for individuals and to the community.[3] Among the negative psychological and social aspects, affecting individuals are couple instability, which in turn may lead to negative effects on health through anxiety, and damages in social relations.[4]

From the community point of view, this situation is not only established but also expected to increase and may lead to aggravated gender discrimination if treatments

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are not more easily accessed.[5] From a demographic perspective, a delay has been observed in the age of women reaching maternity and a decrease in the overall fecundity rate although this cannot be attributed solely to a purely biological problem.[6] Factors such as obesity, taking regular physical activity, substance abuse, or diet[7] may condition the likelihood of subfertility.

The social determinants of health (SDH) are defined as the conditions experienced by individuals may compromise their health and generate inequality.[8] We distinguish structural determinants (cultural and political context, governance, and policy) from intermediate determinants (behavioral, biological, psychological factors and material circumstances). Both of these major groups are, additionally, related through social cohesion or social integration mechanisms, as shown in Figure 1.

The aim is to assess the significance of SDH distribution in relation to natural fertility in subfertile women versus nonsubfertile women.

Subjects and Methods

We designed a prospective comparative study with two groups of women between 18 and 40 years old: a group with subfertile women, referred from primary care to infertility consultation, excluding women without a male partner or with a previous child and a second group formed by primigravidae at their first-gestation consultation, excluding those receiving assisted reproduction techniques to become pregnant. This study was carried out over 1 year in Madrid, Spain.

In estimating sample size, the prevalence of obesity, alcohol, and tobacco consumption in Spain

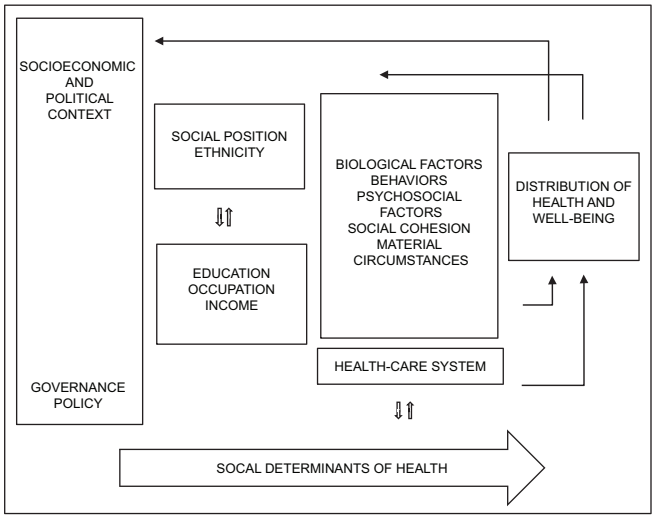

Figure 1: Social determinants of health. Own elaboration from: CSDH. Closing the gap in a generation: Health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health. Geneva, World Health Organization; 2008

women of reproductive age (15–44 years) was taken into account, as declared in the European Health Survey for Spain (EHSS-2014)[9] for a power of 0.80. Calculations were made by means of the GRANMO sample size calculator (https://www.imim.cat/ofertadeserveis/software-public/granmo/).

The analysis included the SDH grouped under biological–metabolic factors, lifestyle or behavioral factors, and environmental and social context factors, following the model by Whitehead and Dahlgren.[10]

Age, ethnic origin (African, American, Asian, or European), the presence of associated morbidity, and weight in the form of body mass index (BMI), as per the WHO, were the variables taken into account under biological factors.

Behavioral or lifestyle factors, including psychological aspects, were analyzed through the consumption of coffee, alcohol, tobacco, other drugs, dietary restrictions, Mediterranean diet products such as fish, and sedentarism and frequency of recreational physical activity (evaluated by five possible answers on frequency). The state of health perceived at the psychological level with regard to energy/vitality was assessed through items 9a (“full of life”), 9e (“lot of energy”), 9g (“worn out”), and 9i (“tired”) in the spanish version of the questionnaire SF-36 v2[11,12] on a scale of 0–100.

Through the environmental and social context factors, the academic level was assessed, in three categories as per the National Classification of Education (CNED-2014)[13] adapted to the 2011 International Standard Classification of Education: levels 0–2, until lower secondary education; levels 3–4, higher secondary education and further; and levels 5–8, higher education. The physical effort required in performing a job was classified as established in the EHSE-2014: seated during most of the day, standing without walking significant distances, carrying weights, and performing tasks involving considerable physical effort. Income level was estimated according to occupation, applying the following scale: high, categories 1–3 of the International Standard Classification of Occupations[14] issued by the International Labour Organization; medium, categories 4–6; and low, categories 7–0.

We studied the relationship between the result variables (subfertile women and nonsubfertile women) and the various factors in the bivariate analysis using Mann–Whitney U-test for quantitative factors as age and logistic regression for categorical factors. Continuous variables were checked for normality with Kolmogorov–Smirnov test. Second, a multivariate analysis was conducted with logistic regression maintaining variables of particular clinical relevance and/or statistical significance in the

bivariate analysis, with two age groups as well, women under 35 and women aged 35 and over. We get the adjusted measure of the effect with a confidence interval (CI) of 95% (95% CI), through the use of Software from IBM SPSS Statistics (https://www.ibm.com/es-es/products/spss-statistics).

In all cases, informed consent was obtained for all information collected and processed. The study has been approved by the Committee for Ethics in Clinical Research at the hospital.

Results

We included consecutively 200 subfertile women (100% of selected cases) in the first group and 197 nonsubfertile women in the other one (we excluded three cases for data loss).

Biological factors

We observed differences in age between both groups ($P < 0.01$). The mean age among subfertile women was 32.8 (4) years, with a median of 33.0, and 59.5% were under 35 years; mean age among nonsubfertile women was 30.8 (4.8) years, with a median of 31 years, and 70.5% were under 35 years. These results are shown in Table 1.

We observed no significant differences ($P = 0.37$) for ethnic origin on comparing the two groups, subfertile women and nonsubfertile women, nor in associated morbidity ($P = 0.53$). Participants were of European origin in 78.6% of cases, while the second largest ethnic group was African (6.3%). In 88.4% of cases, no concomitant illness or chronic treatment was present.

We observed a BMI ≥25 in 42% of all the participants and 17.1% with BMI ≥30; 20.0% of subfertile women were obese. We saw no differences on comparing weight in the two groups ($P = 0.45$), independently of calorie restriction plans ($P = 0.16$). Obesity was associated with the odds ratio (OR): 2.06 (95% CI: 1.08–3.92) with the subgroup of subfertile women aged 35 years or over.

Behavioral factors

We observed no differences in the distribution of consumption of alcohol ($P = 0.88$), tobacco ($P = 0.21$), or beverages containing caffeine ($P = 0.57$) in the two groups, and this proportion was not affected by age group ($P = 0.35$) or ethnic origin ($P = 0.13$). To ensure independence, we analyzed the consumption of alcohol and tobacco jointly ($P = 0.24$).

During the past year, 46.8% of participants said that they had consumed alcohol. The number of drinks per occasion, which was 2.0 (1.1), and the frequency and type of consumption were homogeneous in both groups ($P = 0.39$ and 0.14, respectively). Consumption was mainly beer during the weekend (81.7%). However, 50.3% of Spanish women and 35.2% of other ethnic origin had consumed alcohol ($P = 0.01$).

We observed that 30.4% of participants smoked and that the mean was 11.0 (6.0) cigarettes/day. We found no differences either regarding years of evolution (14.0 years; standard deviation: 5.7). We also found that 46.1% had never smoked and that 23.4% were ex-smokers, a proportion found to be homogeneous in both groups ($P = 0.71$ and 0.61, respectively). However, never having been a smoker was related to OR: 0.51 (95% CI: 0.27–0.96) with the subgroup of subfertile women aged 35 years or over.

We recorded that 70.7% drank coffee or tea on a regular basis. The number of cups daily was 1.3 (1.4). Moreover, we only recorded one positive answer for the consumption of drugs.

Calorie or dietary restriction was reported by 50.2% of participants, and we found no differences between the two groups ($P = 0.16$); calorie restriction, however, was associated to the subgroup of subfertile women of 35 years or over with OR: 0.74 (95% CI: 0.56–0.96) if overweight and with OR: 0.65 (95% CI: 0.52–0.82) if obese.

On collecting data on healthy products in their diet, we found no differences in the consumption of fruit and/or vegetables ($P = 0.13$); differences were only found in the consumption of fish ($P = 0.03$); eating fish once or twice a week was linked to adjusted OR (aOR): 0.40 (95% CI: 0.17–0.95) in the group of subfertile women.

As for regular recreational physical activity, we found differences ($P = 0.01$). Practicing physical activity 3 or 4 days a week was linked to aOR: 0.33 5% CI: 0.15–0.71) in the group of subfertile women. Participants' BMI did not alter the above effect ($P = 0.84$).

The score for the perceived health condition on the psychological plane, through the energy/vitality index, also gave rise to differences ($P < 0.01$), unmodified by ethnic origin ($P = 0.73$). The scores and the respective aOR are shown in Table 2, together with a summary of the distribution of the remaining behavioral factors.

Contextual factors

No differences were observed in comparing contextual factors for subfertile women and nonsubfertile women with regard to academic level ($P = 0.94$) nor with regard to physical effort at the workplace ($P = 0.53$) or the current unemployment rate ($P = 0.57$).

The social hierarchy structure was likewise seen to be homogeneous in both groups, assessed through the income level earned from employment ($P = 0.93$). No

modification due to ethnic origin was observed in the above, except in unemployment ($P < 0.01$).

We found that 77.2% of participants did not have higher education, and the percentage of unemployment registered was 7.6% (2.5% of Spanish women and 25.8% of other ethnic origins). About 75.9% of women work sitting or standing; only 2.8% of them have positions with considerable physical effort. The overall proportion of low income was 20.4%.

Table 1: Biological factors: subfertile women versus nonsubfertile women comparison

	Subfertile women (*n*=200)	Nonsubfertile women (*n*=197)	*P*
Age			
Mean (SD)	32.86 (4.07)	30.84 (4.81)	<0.01*
<35 years (%)	59.50	70.55	
Ethnic origin			
European (%)	80.50	76.64	0.37
Morbidity (%)	12.30	14.60	0.53
BMI (%)			0.45
<18.5	2.50	3.56	
18.5-24.9	53.00	56.85	
25-29.9	24.50	25.38	
>30	20.00	14.21	

*Statistical significance $P<0.05$. *P* from Mann-Whitney U-test for age. *P* from logistic regression for others. BMI=Body mass index, SD=Standard deviation

Discussion

The aim of our study was to assess the significance of SDH distribution in relation to natural fertility in subfertile women versus nonsubfertile women. The main novelty in our study was based on a global approach and vision of the different SDH related to subfertility, as opposed to the existing literature. We found that woman's age and certain living conditions such as an unhealthy diet or a sedentary lifestyle can negatively influence fertility.

The groups that we compared took into account women with difficulties trying to achieve a pregnancy and women who did not have any difficulties getting pregnant: this was our primary endpoint. We tried to emphasize that even if having difficulties to achieve a pregnancy may be a real health problem, it may not necessarily mean that it is permanent or irreversible. Hence, to try to define this problem, we used the terminology explained in our manuscript, trying to avoid the classical "sterile" or "infertile," as it may imply a pejorative or downgrading implications in itself.

Age was different between the two groups studied; subfertile women were older on average than nonsubfertile women. With regard to fertility, age is a principal factor both from a biological point of view, as reproductive capacity declines with age, and from

Table 2: Behavioral factors: subfertile women versus nonsubfertile women comparison

	Subfertile women (*n*=200)	Nonsubfertile women (*n*=197)	*P*	OR	aOR (95% CI)
Alcohol (%)					
Drinkers	46.50	47.20	0.88		
Tobacco (%)					
Smokers					
Daily	28.50	32.48	0.21		
Never	47.00	45.17			
Ex	24.50	22.30			
Caffeine (%)					
Coffee, tea	69.50	72.10	0.57		
Feeding					
Intake restriction (%)	54.37	46.90	0.15		
Healthy food			0.03*		
Fish 1-2 times a week (%)	26.90	46.40		0.39	0.40 (0.17−0.95)
Physical activity					
Regular exercise			0.01*		
Exercise 3-4 days a week (%)	30.62	45.17		0.38	0.33 (0.15−0.71)
Vitality (SF-36v2®)					
"Full of life" (SD)	82.91 (13.78)	85.54 (15.50)	<0.01*	0.74	0.72 (0.59−0.88)
"Lot of energy" (SD)	76.99 (18.88)	71.35 (19.15)		1.30	1.32 (1.13−1.55)
"Worn out" (SD)	54.85 (28.65)	50.26 (33.31)		1.13	1.13 (1.04−1.23)
"Tired" (SD)	55.00 (26.24)	64.15 (22.94)		0.88	0.80 (0.72−0.89)

*Statistical significance $P<0.05$. *P* from logistic regression. OR=Odds ratio, aOR=Adjusted OR of multivariate analysis, SD=Standard deviation, CI=Confidence interval

a social point of view; age is associated with our role in society. Moreover, it is clearly established that the decline in fertility accelerates dramatically after the age of 35 years.

The trend, shared with other European countries, is to delay motherhood into the thirties, a tendency that has been increasing in Spain since the 1970s. Age and the duration of subfertility are two of the principal factors in reproductive forecasting.[15] If pregnancy is not achieved after one year of unprotected intercourse (or after 6 months in women over 35), it is recommended a medical check.

The influence of ethnic origin on natural fertility or in *in vitro* fertilization (IVF) success is not well known.[16] In our study, we found no differences, though both groups included a majority of women of European origin. Therefore, ethnic origin may condition other behaviors such as the intake of alcohol and contextual factors, so it could be indirectly related to fertility through variables such as religion, values, or cultural preferences.

The prevalence of obesity in Spain among women of reproductive age stands at around 15%–20%. It is likewise related to subfertility through several mechanisms such as dysfunctional ovulation.[17] In fact, weight loss is associated with improved hormonal balance and ovulation rate.[18]

Our data regarding obesity are similar to those in the EHSE-2014, but our most outstanding finding was that the presence of obesity doubles the risk of being of subfertile in women of 35 years or over. Similarly, restricting calorie intake reduced the risk by 35% in obese women and by 26% in overweight women, for the same subgroup.

As for diet composition, the inclusion of fish once or twice a week was associated with a 60% reduction in the risk of subfertility according to our study. The inclusion of fruit and/or vegetables did not yield the above result. Eating healthy products may be restricted by economic barriers but also by cultural barriers which are more easily modified. The current recommendations for healthy eating habits include oily fish at least twice weekly and at least four portions of fruit, vegetables, or salad daily.[19]

Regarding regular physical exercise, we also obtained significant results: regular physical exercise 3 or 4 days per week led to a 67% decrease in the risk of subfertility, according to our data. Moderate physical exercise enhances the likelihood of pregnancy specifically in obese or overweight women.[20] The current recommendations given by the Australian Fertility Society prescribe 30 min of moderate exercise prior to conception, preferably every day, and to include regular vigorous activity if possible.

Substances such as alcohol or tobacco have been associated with adverse effects on reproduction. However, on the consumption of caffeine, there are no such conclusive results.[21]

It is significant to highlight that half of our patients had consumed alcohol during the last year, which is a considerably smaller proportion than those found in other studies.[22] The above findings may be attributed to a bias (suspected underdeclaration) stemming from cultural or social reasons. Alcohol has been associated with subfertility through several mechanisms such as hormonal changes. These effects have been also described in IVF cycles.[23]

Nevertheless, our data regarding tobacco are quite similar to those of other groups: almost one-third of participants smoked daily. This behavior is probably explained by a higher tolerance toward the consumption of tobacco in our environment. According to our results, women who had never smoked were at a 49% lower risk of finding themselves among the subfertile women of 35 years or over. There is conclusive evidence in the literature of the harmful effects of tobacco on reproduction.[24]

On the psychological aspect, we assessed the individual's degree of well-being with herself and with her surroundings, with regard to their fertility status. These dimensions encompass competences such as resilience, adaptability, or the observance of healthy habits. Among the negative items, "tired" and "worn out," we observed a greater variability than among the positive items. The interpretation of the aOR was found to be contradictory and of little clinical value, as both positive and negative items worked as protective factors and risk factors, respectively, and the values are very close to one. However, participants' self-assessment was found to be patently positive. The opposite, that is, a negative self-assessment, would lead to psychological distress producing not only personal suffering[25] but also possibly a negative impact on the family and social circle.

As for contextual factors, our results did not show differences between subfertile women and nonsubfertile women. A poor level of education is the main barrier to accessing the labor market but not the only one. Lower qualifications lead to jobs with less responsibility and requiring greater physical effort and probably less stable and with lower incomes, all of which create a social gradient. There are a few studies that point to a relationship between the social gradient and adverse reproductive events such as spontaneous

abortion.[26] In our study, social hierarchy did not appear to be determinant in fertility issues though we should remember that in Spain, we benefit from a national health system that covers all citizens.

Different groups have reported similar results for most of the analyzed variables, with the exception of alcohol. However, these studies present great heterogeneity due to the way variables were evaluated, something we tried to mitigate by a joint evaluation, as we did in our study.

Conclusions

We confirm that the distribution of SDH in natural fertility is not altogether homogeneous.

With regard to the limitations to this study, we may mention a hypothetical response bias, limited sample size, and the lack of randomization. However, this research reflects real-life data, retrieving data from routine clinical practice, and trying to guarantee that these data were as homogenous as possible due to a careful study design. Moreover, we were extremely cautious when defining the variables to consider and analyze, so that sample size would have a minimal impact on the results. On the other hand, we provided an integrated evaluation of the SDH and fertility at the same time. Weight control by means of restricting calorie intake, greater consumption of healthy foods such as fish, regular physical exercise, and lower age are positively associated with fertility. Population-level intervention is possible to improve women's health, as these are modifiable factors. Ethnic origin can be considered as a relevant factor, as it may condition the distribution of other determinants.

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Conflicts of interest

There are no conflicts of interest.

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