Factors associated with pregnancy and live birth after in-vitro fertilization techniques in Albania, 2006-2012

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Abstract

Aim: The aim of this study was to retrieve information regarding the results of in-vitro fertilization procedures (IVF) and factors associated with pregnancy and live birth after IVF procedures in order to shed light into this under-researched topic in Albania.
Methods: We included 246 infertile couples who showed up at the "Iakentro" IVF clinic during 2006-2012. Estradiol level, endometrium thickness and the number of embryos transferred were measured in all cases. In addition, basic socio-demographic information was collected. Binary logistic regression was used to assess the association of socio-demographic and laboratory parameters with pregnancy and live birth after IVF.
Results: The rate of pregnancy after IVF was 45%. Among these, 67.3% of pregnancies resulted in live births. In our total sample, the rate of live births was 30.3% whereas the abortion rate after IVF was 14.7%. Upon multivariable adjustment, the higher number of embryos transferred was significantly associated with higher odds of pregnancy and live birth after IVF.
Conclusions: Our findings indicate that pregnancy and live birth rates after IVF in Albania are comparable to those in developed countries. In the future, information regarding IVF procedures and their results in Albania should be more complete and accurate in order to ensure the quality of IVF services and improve the regulation of this sector.

Keywords: Albania, infertility, in-vitro fertilization procedures, live birth, pregnancy.

Introduction

Infertility is defined as failure to achieve pregnancy after at least 12 months of regular unprotected sexual intercourse for women aged up to 35 years or after 6 months for women aged more than 35 years (1).

Infertility, which constitutes a permanent problem with worldwide implications, has been proclaimed as the challenge of the millennium (2). It might affect 50-80 million women across the globe, and this might be just an underestimation (3). In developing countries, the incidence of secondary infertility is estimated up to 50% (4).

There are numerous known and unknown factors which might affect the capabilities of human reproductive system. The single most important independent factor affecting the couples' chances to conceive and give birth either naturally or artificially is the age of the woman. This issue is gaining increasing importance in the context when women are postponing their maternity, a tendency made obvious during last decades (5). The reasons for delaying pregnancy include the use of contraception, education and career issues and marriage at older ages (6). Factors associated with infertility could be the paternal age (7-9), duration of efforts to remain pregnant (10), contraceptive use (11), environmental and occupation pollutants (12), obesity (13), lifestyle issues such as smoking (14), caffeine use (15) and alcohol (16), stress and anxiety (17), and infectious diseases (18).

Global trends of infertility are being increasingly studied. According to a literature review, the yearly prevalence of infertility among women aged 20-44 years varied between 3.5%-16.7% in the developed countries and between 6.9%-9.3% in developing countries whereas the median prevalence was 9%. This means that around 72 million women aged 20-44 years in the world were infertile during 1988-2005 (19). Parallel with the global reduction of fertility and the increasing of demand for medical treatment of it, the percentage of women with one or two children who are at risk of remaining pregnant is reduced since 1990 literally in every region of the world, resulting in a reduction of the share of women affected by secondary infertility (20).

The information regarding the prevalence of infertility in Albania is very limited. However, in 2012 the Minister of Health reported that approximately 12% of Albanian couples face difficulties in conceiving (21). Information regarding the factors associated with infertility and about indicators of the results of IVF procedures and factors associated with the success of such procedures is currently lacking.

Causes of infertility are different and can be classified into female or male causes, mix or idiopathic ones. The treatment of these causes not always results in a live birth. In cases when conventional treatments fail, the assisted reproduction techniques (ART) are suggested. These techniques have started to being used since 2003 after the respective legislation was approved and there are now at least 10 private clinics offering such services in Albania. However, the information from these clinics is difficult to be obtained due to informality issues.

Even though scientific information regarding infertility is abundant in the international literature, in Albania such information is lacking or, in the best of cases, is extremely limited, a situation which is not helpful for policymakers to take the appropriate measures for changing or improving the potential problems associated with this phenomenon.

In this context, the aim of the present study is the retrieval of the information regarding the results of the IVF procedures and factors associated with pregnancy and live birth after IVF in order to shed light upon this under researched topic in our country.

Methods

Study design

This was a cross-sectional study, covering the time period 2006-2012.

Study population and sampling

The study population included all infertile couples which showed up at the "Iakentro" infertility clinic during 2006-2012 and for whom there was information available regarding certain socio-demographic and laboratory parameters. The inclusion criterion was the showing up of the couples at our clinic for the treatment of problems impeding them from having the first child or having another

child, despite of their place of residence. This is why, apart from infertile couples residing in Albania, in our study were included some couples living abroad as well. As a result, no sampling technique was employed since we included all infertile couples showing up at our clinic during the aforementioned 7-year time period of the study. In total, from the 473 infertile couples showing up at our clinic during this period of time, only for 246 of them there was available complete information and therefore this is our study population..

Data collection

The data collection was done during the initial assessment (interview) of the infertile couple as well as through various laboratory and clinical examinations. The basic socio-demographic data such as age of the woman, place of residence and the level of education were retrieved during the initial assessment.

Besides the interview, the following examinations were performed: endovaginal ultrasound, measurement of hormones in day two and six of the menstrual cycle; hysterosalpingography. In these days the level of estradiol and thickness of endometrium was measured. The level of estradiol was measured in serum (blood) and analyzed in MINIVIDAS equipment using the immunofluorescence methods. The thickness of endometrium was measured by ultrasound probe with baseline, in millimeters, respecting its echogenic borders. Values of endometrium thickness reported in the tables of this study refer to its measurement at the day of the eggs pick-up.

Statistical analysis

For numerical variable the measures of central tendency (arithmetic mean) and dispersion (standard deviation) were reported. For categorical variables absolute numbers and their respective percentages were reported.

For the assessment of the associations between variables the appropriate statistical tests were used. For numerical normally distributed variables the student "t" test was used. For comparing of categorical variables, the chi square test was used.

To determine the factors associated with pregnancy and live birth after IVF procedures the Binary Logistic Regression (BLR) was used. We employed three models of BLR: in Model 1 we controlled (adjusted) only for the effect of age; in Model 2 we additionally controlled for place of residence and education level; in Model 3 we simultaneously controlled for all of the potential confounders presented in the tables.

In all cases, a value of $P<0.05$ was considered as statistically significant. The whole analysis was performed using the SPSS (Statistical Package for Social Sciences) statistical package, version 17.

Results

The mean age of participants was 32.9 years (±5.1 years). There was a statistically significant increase of 2.1 years in the mean age of women showing up at the beginning and the end of the study period (data

Table 1. Distribution of the subjects under study according to the results of IVF treatment

Variable	Number	Percentage
Results after IVF treatment		
Negative (*pregnancy not achieved*)	127*	55.0
Positive1 (*pregnancy achieved, one fetus*)	89	38.5
Positive 2 (*pregnancy achieved, two fetuses, multiple pregnancy*)	9	3.9
Positive 3 (*pregnancy achieved, ≥3 fetuses, multiple pregnancy*)	6	2.6
Results among IVF pregnant women (n=104)		
Live birth	70	67.3
Abortion	34	32.7
Overall results of IVF treatment		
Negative result (*no pregnancy achieved*)	127	55.0
Positive results (*pregnancy achieved*)	104	45.0
Live birth (*pregnancy ended in live birth*)	70	30.3†
Abortion (*pregnancy ended in abortion*)	34	14.7‡

* Discrepancies with the total number of subjects are due to missing data.
† Proportion of women experiencing a live birth among all women under study.
‡ Proportion of women experiencing an abortion among all women under study.

not shown). Regarding the results of IVF procedures, in 55% of cases the procedures didn't achieve pregnancy whereas in 45% they did so. Among those who remained pregnant after IVF, 67.3% gave birth to at least on living child, whereas 32.7% resulted in abortion. In our total sample, the rate of live birth after IVF was 30.3% whereas the abortion rate was 14.7% (Table 1).

Table 2 presents data on pregnancy and live birth after IVF according to socio-demographic and laboratory parameters. Two-thirds of infertile couples resided in urban areas and the same proportion were 35 years of age or younger. One in five infertile women had 8 years or education or less. The prevalence of primary infertility was 77.3%. Also, in almost two-thirds of cases (65.3%) three to four embryos had been transferred.

Table 2. Distribution of pregnancy and live births after IVF by socio-demographic factors and laboratory parameters

Variable	Total	Pregnancy		Live birth	
		No	Yes	No	Yes
Residence		[A]		[A]	
Urban	156 (66.7)	87 (58.8)*	61 (41.2)	109 (73.6)	39 (26.4)
Rural	78 (33.3)	34 (47.2)	38 (52.8)	46 (63.9)	26 (36.1)
Age-group		[B]		[B]	
≤35 years old	165 (67.3)	78 (50.0)	78 (50.0)	102 (65.4)	54 (34.6)
>35 years old	80 (32.7)	48 (64.9)	26 (35.1)	58 (78.4)	16 (21.6)
Education level		[B]		[B]	
8-years	36 (16.4)	14 (42.4)	19 (57.6)	17 (51.5)	16 (48.5)
High school	94 (42.9)	57 (64.8)	31 (35.2)	70 (79.5)	18 (20.5)
University	89 (40.6)	42 (50.0)	42 (50.0)	58 (69.0)	26 (31.0)
Type of infertility		[A]		[A]	
Primary	187 (77.3)	96 (55.2)	78 (44.8)	118 (67.8)	56 (32.2)
Secondary	55 (22.7)	31 (58.5)	22 (41.5)	42 (79.2)	11 (20.8)
Number or transferred embryos		[C]		[C]	
1-2 embryos	76 (34.7)	56 (73.7)	20 (26.3)	64 (84.2)	12 (15.8)
3-4 embryos	143 (65.3)	64 (44.8)	79 (55.2)	88 (61.5)	55 (38.5)
Protocol		[A]		[A]	
P2	107 (43.7)	50 (48.5)	53 (51.5)	67 (65.0)	36 (35.0)
P5	138 (56.3)	76 (59.8)	51 (40.2)	93 (73.2)	34 (26.8)
Estradiol level		[D]		[A]	
<842	82 (33.3)	45 (60.8)	29 (39.2)	55 (74.3)	19 (25.7)
843-1499	82 (33.3)	47 (59.5)	32 (40.5)	57 (72.2)	22 (27.8)
>1499	82 (33.3)	35 (44.9)	43 (55.1)	49 (62.8)	29 (37.2)
Endometrium thickness		[A]		[A]	
<9mm	48 (24.1)	24 (54.5)	20 (45.5)	34 (77.3)	10 22.7)
10-11mm	97 (48.7)	49 (52.7)	44 (47.3)	64 (68.8)	29 (31.2)
>11mm	54 (27.1)	26 (49.1)	27 (50.9)	33 (62.3)	20 (37.7)

* Row percentages. Discrepancies with the total number of subjects are due to missing data.
[A] P>0.05 (chi-square test).
[B] P<0.05 (chi-square test).
[C] P<0.001 (chi-square test).
[D] P=0.087 (chi-square test).

Tables 3 and 4 display the associations of pregnancy and live birth after IVF procedures with socio-demographic and laboratory parameters. In age-adjusted analysis (Model 1 in both tables), the likelihood of pregnancy and live birth was significantly higher among women aged d" 35 years (OR=1.8 and OR=1.9, respectively, P<0.05) compared to women over 35 years old. The odds

of live birth were significantly higher among low education women compared to those having university education (OR=2.3, P=0.055, borderline significance). In addition, women with 3-4 transferred embryos were significantly more likely to remain pregnant after IVF (OR=3.2, P<0.001; Table 3) and to give birth to a living baby (OR=3.1; P=0.002; Table 4) compared to women who received 1-2 embryos. The other associations resulted not statistically significant.

In multivariable-adjusted analysis (Model 3 in Table 3 and in Table 4), the general picture remained more or less the same, but the association with age turned not significant. The association with education was of borderline significance regarding pregnancy, whereas the association with the number of transferred embryos retained its significance (for live birth there was borderline significance), but the associations weakened (OR=2.1, P=0.019 for the association with pregnancy; Table 3 and OR=2.1, P=0.082 for the association with live birth, Table 4).

Table 3. Association of socio-demographic and laboratory factors with pregnancy after IVF treatment: odds ratios (ORs) from binary logistic regression

Variable	Model 1		Model 2		Model 3	
	OR (95% CI)*	P	OR (95% CI)	P	OR (95% CI)	P
Residence						
Urban	1.0 (reference)	0.107	1.0 (reference)	0.018	1.0 (reference)	0.095
Rural	1.6 (0.9-2.8)		2.8 (1.2-6.5)		2.3 (0.9-6.1)	
Age-group						
≤35 years old	1.8 (1.0-3.3)	0.035	2.0 (1.1-3.8)	0.029	1.4 (0.6-3.1)	0.420
>35 years old	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Education level		**0.020 (2)**†		0.020 (2)		**0.076 (2)**
8-years	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
High school	0.7 (0.2-1.7)	0.380	0.7 (0.3-1.7)	0.380	0.6 (0.2-1.9)	0.427
University	1.7 (0.6-5.3)	0.338	1.7 (0.6-5.3)	0.338	1.6 (0.4-6.2)	0.483
Type of infertility						
Primary	1.1 (0.6-2.0)	0.859	0.9 (0.5-1.9)	0.825	1.0 (0.4-2.3)	0.990
Secondary	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Number or transferred embryos						
1-2 embryos	1.0 (reference)	<0.001	1.0 (reference)	0.001	1.0 (reference)	0.019
3-4 embryos	3.2 (1.7-5.9)		2.9 (1.5-5.6)		2.3 (1.2-4.8)	
Protocol						
P2	1.4 (0.8-2.5)	0.212	1.6 (0.8-2.8)	0.155	1.5 (0.8-3.2)	0.238
P5	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Estradiol level		**0.143 (2)**		**0.293 (2)**		**0.280 (2)**
<842	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
843-1499	0.9 (0.5-1.8)	0.935	1.0 (0.5-2.0)	0.905	1.0 (0.4-2.3)	0.998
>1499	1.7 (0.9-3.3)	0.103	1.6 (0.8-3.4)	0.207	1.8 (0.8-4.4)	0.168
Endometrium thickness		**0.924 (2)**		**0.910 (2)**		**0.888 (2)**
<9mm	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
10-11mm	0.9 (0.4-1.9)	0.862	1.2 (0.5-2.6)	0.729	0.9 (0.4-2.3)	0.942
>11mm	1.1 (0.4-2.4)	0.863	1.2 (0.5-3.0)	0.674	1.2 (0.5-3.1)	0.734

Model 1: adjusted only for age.
Model 2: adjusted for place of residence and level of education.
Model 3: adjusted simultaneously for all the variables presented in the table.
* Odds ratios (ORs) and 95% confidence intervals (in brackets).
† Overall p-values and degrees of freedom (in brackets).

Table 4. Association of socio-demographic and laboratory factors with live birth after IVF treatment: results from Binary Logistic Regression

Variable	Model 1		Model 2		Model 3	
	OR (95% CI)*	P	OR (95% CI)	P	OR (95% CI)	P
Residence						
Urban	1.0 (reference)	0.084	1.0 (reference)	0.337	1.0 (reference)	0.553
Rural	1.6 (0.9-3.4)		1.6 (0.6-4.0)		1.4 (059-4.2)	
Age-group						
≤35 years old	1.9 (1.0-3.7)	0.047	2.3 (1.1-4.7)	0.025	1.4 (0.6-3.5)	0.449
>35 years old	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Education level		**0.006 (2)**†		0.025 (2)		**0.020 (2)**
8-years	2.3 (1.0-5.4)	0.055	1.5 (0.5-4.9)	0.472	2.3 (0.6-9.8)	0.248
High school	0.6 (0.3-1.1)	0.095	0.5 (0.2-1.1)	0.066	0.5 (0.2-1.3)	0.145
University	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
Type of infertility						
Primary	1.7 (0.8-3.6)	0.168	1.6 (0.7-3.8)	0.270	1.6 (0.6-4.2)	0.391
Secondary	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Number or transferred embryos						
1-2 embryos	1.0 (reference)	0.002	1.0 (reference)	0.011	1.0 (reference)	0.082
3-4 embryos	3.1 (1.5-6.3)		2.6 (1.2-5.6)		2.1 (0.9-4.7)	
Protocol						
P2	1.3 (0.7-2.3)	0.390	1.3 (0.0.7-2.6)	0.382	1.5 (0.8-3.2)	0.332
P5	1.0 (reference)		1.0 (reference)		1.0 (reference)	
Estradiol level		**0.374 (2)**		**0.758 (2)**		**0.930 (2)**
<842	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
843-1499	1.0 (0.5-2.1)	0.933	1.1 (0.5-2.4)	0.896	1.0 (0.4-2.5)	0.979
>1499	1.5 (0.8-3.1)	0.225	1.3 (0.6-2.9)	0.494	1.2 (0.5-2.9)	0.758
Endometrium thickness		**0.427 (2)**		**0.152 (2)**		**0.129 (2)**
<9mm	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-
10-11mm	1.4 (0.6-3.2)	0.465	2.1 (0.8-5.6)	0.053	2.1 (0.7-5.8)	0.166
>11mm	1.8 (0.7-4.5)	0.197	2.9 (1.0-8.3)	0.043	3.2 (1.1-9.9)	0.043

Model 1: adjusted only for age.
Model 2: adjusted for place of residence and level of education.
Model 3: adjusted simultaneously for all the variables presented in the table.
* Odds ratios (ORs) and 95% confidence intervals (in brackets).
† Overall p-values and degrees of freedom (in brackets).

Discussion

The present study for the first time presents information regarding the results of IVF procedures in Albania. The main findings of our study are summarized as follows: the rate of pregnancy after IVF procedures was 45%. Among those who remained pregnant, 67.3% experienced a live birth whereas the remaining 32.7% ended in abortion. The overall rate of live birth after IVF procedures was 30.3% and the factors significantly associated with pregnancy and live birth after IVF were the level of education and number of transferred embryos. However, despite not achieving statistical significance for other independent factor included in the study, the clinical significance of the findings is clear: women d"35 years old, those highly educated, women with primary infertility, those being transferred 3-4 embryos, those treated with P2 protocol, those with higher levels of estradiol and women with thicker endometrium were more likely to remain pregnant and to give a live birth after IVF procedures compared with their respective counterparts.

Infertility is largely understudied in Albania, whereas its treatment through contemporary methods of assisted reproductive techniques (ART) is being implemented on large scale only recently, favored

by the increasing of the proportion of infertile couples and the "liberal" legislation in place regulating such procedures.

The legal basis for regulating infertility issues in Albania is to be found in the Law Number 8876, dated 04.04.2002 "On reproductive health", and changed with the Law Number 10137, dated 11.05.2009 (22), which regulates all the activities of reproductive health, in the public and private sector, through protecting the reproductive rights of the individual and the couple in accordance with national and international policies and practices. Point (ë), article 3 of the law refers to the prevention and treatment of *infertility*. Article 10 guarantees to all individuals and couples the right to benefit from the use of affordable and acceptable methods for the correction of infertility. Section V of the law deals with the assisted reproductive techniques, which includes clinical and biological methods which enable the in-vitro conception, embryos' transferring and artificial insemination as well as all other similar techniques which allow for the reproduction process to occur apart from the natural processes (22).

In essence, the law "On reproductive health" in Albania does not impede any in-vitro fertilization technique, and as so, it literally allows egg donation, sperm donation, or embryo donation and it does not limit the number of the later which can be transferred and this is the reason why the number of infertile couples residing abroad and seeking help through IVF treatment in Albania is increasing. Even though there is no scientific research, this issue has recently been brought into the attention by the media. For example, a recent article reported that a considerable number of couple coming from different countries have decided to treat their infertility in Albania due to relatively lower prices, liberal legislation in place which allows the picking-up and transferring of a high number of embryos and the favorable religious climate as well as the lack of waiting times to treatment (23).

In Albania there are no exact figures regarding the prevalence of infertility. Meanwhile, the Ministry of Health reported that around 12% of couples in this country face some sort of difficulties to conceive (21), but according to gynecologists this number could jump up to 15% (24). In Tirana, during 2004-2012, among approximately 33 thousand births occurring in "Koco Gliozheni" maternity hospital, 497 women benefited pregnancy from ART techniques. According to these numbers, it is estimated that across the country there are about 1000 babies born through ART procedures during the same period (21). Other data regarding infertile couples are scarce.

The socio-demographic changes which have taken place in Albania during the last 23 years suggest for lifestyle and morbidity and mortality trends similar to those observed in the developed world: the increasing of sedentary lifestyle, increasing of calorie intake, increasing of chronic morbidity (25-30), decreasing of fertility rates (31) and delaying of first pregnancy. Under these conditions, it is estimated that the prevalence of infertility in our country is on the rise and, therefore, it is indispensable to obtain detailed information regarding this issue.

Some of the findings of our study are in concordance with those reported in the literature. We observed a significant increase of 2.1 years in the mean age of infertile women presenting at our clinic in the beginning and the end of the 7-year period of the study, which implies that women are delaying in time the moment of their first pregnancy, a finding similar to that reported in the literature (5,6). The main problem with this finding is that women are not really aware of the importance of age for achievement of pregnancy and first live birth and by doing so they delay their first pregnancy until it is too late. This is favored by the image being conveyed by the mass media which advertises the pregnancy of famous persons occurring at advanced ages, even though only a few know that these pregnancies were achieved artificially and not naturally. For this reason, it is very important to educate women regarding age as a crucial factor for achieving pregnancy.

On the other side, we reported that higher levels of estradiol and thicker endometrium was associated with higher likelihood of pregnancy and live birth after IVF (even though we didn't succeed to observe significant results, still the trend and clinical significance is clear, as we mentioned earlier in this section), findings which are supported by the literature as well (32,33).

In our study we reported that transferring of 3-4 embryos was significantly associated with increased likelihood of pregnancy and live birth after IVF. Literature findings are ambiguous regarding this issue.

For example, a recent article (34) reported that, after assessment of 124148 IVF cycles resulting in 33514 live births (or a live birth rate of 27% per cycle), the likelihood of live birth were higher among women aged 40 or older compared to those less than 40 years old when two embryos were transferred compared to one embryo, but the rates of live births did not increase when three or more embryos were transferred, whereas the risk of birth associated adverse effects increased, suggesting that the transferrin of three or more embryos should be avoided (34). Yet, another study reported similar findings to those reported by us (35). However, we admit that the increasing of the number or transferred embryos can increase the risk of multiple pregnancy and twin or triple live births, which are accompanied by their own considerable costs for the individual and the society.

The level of live births after IVF procedures in our study was comparable to that reported in the literature. We found that 30.3% of infertile couples undergoing IVF procedures managed to give birth to at least one living baby after a cycle of treatment. In literature this level is being reported similarly to our finding. For example, in a study among 750 infertile patients reported, after a cycle of treatment, a live birth rate of 21.4% in 1997, 23.3% in 1998, 30% in 1999 and 25% in 2000 (36), around 31% was reported by another study (37), and 27% was yet reported by an additional large cohort study (34) This level of close comparability means that the IVF procedures in Albania are being performed using a similarly developed and modern infrastructure and employing a similarly appropriately trained medical staff as in developed countries.

In summary, we conclude by stating that the prevalence of infertility is maybe quickly increasing in this Southeast European country, closely following the important "western type" changes of lifestyle, morbidity patterns, as well as reduction of fertility rates and delaying of first pregnancy. In this perspective, Albania is following the trends observed in developed countries, which implies that infertility will be an increasing concern to our society and an increasingly important topic of therapeutic medicine, favored by the liberal legislation in this regard. Treatment of infertility through IVF techniques in our country is still in its infancy but, however, the results of these procedures are still comparable with those observed in developed world. Despite this, the information regarding the activities of private clinics or hospitals offering these procedures must and should be much more accurate and complete in the future in order to guarantee the quality of IVF services offered and the better regulation of this rapidly expanding market in Albania.

References

1. Definition of infertility and recurrent pregnancy loss. The Practice Committee of the American Society for Reproductive Medicine. The American Society for Reproductive Medicine, Birmingham, Alabama. Fertil Steril 2008; 90:S60.

2. Vayena E, Rowe PJ, Griffin PD (eds). Medical, ethical & social aspects of assisted reproduction. Current practices & controversies in assisted reproduction: Report of a WHO meeting, 2001: Geneva, Switzerland.

3. World Health Organization. Infertility: a tabulation of available data on prevalence of primary and secondary infertility. Geneva, WHO, Programme on Maternal and Child Health and Family Planning, Division of Family Health, 1991.

4. Cates W, Farley TM, Rowe PJ. Worldwide patterns of infertility: is Africa different? Lancet 1985; 2:596-598.

5. Mathews TJ, Hamilton BE. Delayed Childbearing: More Women Are Having Their First Child Later in Life. Hyattsville, MD: National Center for Health Statistics; 2009. NCHS Data Brief; No. 21.

6. Mills M, Rindfuss RR, McDonald P, TeVelde E, ESHRE Reproduction and society Task Force. Why do people postpone parenthood? Reasons and social policy incentives. Hum Reprod Update 2011; 7:848-860.

7. Speroff L. The effect of aging on fertility. Curr Opin Obstet Gynecol 1994; 6:115-120.

8. Vermeulen A. Environment, human reproduction, menopause and andropause. Envir Health Perspect 1993;101(Suppl 2):91-100.

9. Sartorius GA, Nieschlag E. Paternal age and reproduction. Hum Reprod Update 2010; 16:65-79.

10. Schwartz D, Mayaux MJ. Female fecundity as a function of age: results of artificial insemination of 2193 nulliparous women with azoospermic husbands. Federation CECOS. N Engl J Med 1982; 306:404-406.

11. Hassan MAM, Killick SR. Is previous use of hormonal contraception associated with a detrimental effect on subsequent fecundity? Hum Reprod 2004; 19:344–351.

12.Rowland AS, Baird DD, Weinber CR, et al. Reduced fertility among women employed as dental assistants exposed to high level so nitrous oxide. N Engl J Med 1992; 327:993-997.

13.Ryley DA, Bayer SR, Eaton A, et al. Influence of body mass index (BMI) on the outcome of 6,827 IVF cycles. Fertil Steril 2004; 82:S38-S39.

14.Bolumar F, Olsen J, Boldsen J. Smoking reduces fecundity: a European multicenter study on infertility and subfecundity. European Study Group on Infertility Subfecundity. Am J Epidemiol 1996; 143:578-587.

15.Bolumar F, Olsen J, Rebagliato M, et al. Caffeine intake and delayed conception: a European multicenter study on infertility and subfecundity. European Study Group on Infertility Subfecundity. Am J Epidemiol 1997; 145:324-334.

16.Hakim RB, Gray RH, Zacur H. Alcohol and caffeine consumption and decreased fertility. Fertil Steril 1998; 70:632-637.

17.Domar AD. Infertility and the mind/ body connection. Female Patient 2005; 30:24–28.

18.Thonneau P. Femaile and male risk factors: results of a case control study. Hum Reprod 1992; 7:55-58.

19.Boivin J, Bountin L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Human Reprod 2007; 22:1506-1512.

20.Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med 2012; 9:12.

21. Konferenca Rajonale "Fertiliteti i ndihmuar medikalisht", Tiranë, Tetor 2012. Njoftim për shtyp i Ministrisë së Shëndetësisë (In Albanian). Available at: http:/ / www.moh.gov.al/ index.php/ shtator-2012/ 524-fillon-punimet-konferenca-rajonale-fertiliteti-i-ndihmuar-medikalisht-mjekesia-e-se-ardhmes. Accessed on February 2013.

22.Qendra për cështje të informimit publik. Ligji numër 8876, datë 04.04.2002 "Për shëndetin riprodhues" (In Albanian). Available at: http:/ / www.infocip.org/ al?p=6843. Accessed on February 2013.

23.Shqipëria, "destinacion turistik" për bebe në epruvetë. Gazeta Shqip, 8 Mars 2013 (In Albanian). Available at:http:/ / gazeta-shqip.com/ lajme/ 2013/ 02/ 18/ shqiperia-destinacion-turistik-per-bebe-ne-epruvete/ . Accessed on March 2013.

24.Rreth 15 për qind e shqiptarëve nuk mund të sjellin në jetë një fëmijë në rrugë natyrale. Gazeta Shqip, 8 Mars 2013 (In Albanian). Available at: http:/ / gazeta-shqip.com/ lajme/ 2012/ 10/ 19/ riprodhim-i-asistuar-edhe-ne-spitalet-private/ . Accessed on March 2013.

25.Gjonça A, Bobak M. Albanian paradox, another example of protective effect of Mediterranean lifestyle? Lancet 1997; 350:1815-1817.26. Shapo L, Pomerleau J, McKee M, Coker R, Ylli A. Body weight patterns in a country in transition: a population-based survey in Tirana City, Albania. Public Health Nutr 2003; 6:471-477.1.

26.Shapo L, Pomerleau J, McKee M, Coker R, Ylli A. Body weight patterns in a country in transition: a population-based survey in Tirana City, Albania. Public Health Nutr 2003; 6:471-477.

27.Shapo L, Pomerleau J, McKee M. Epidemiology of hypertension and associated cardiovascular risk factors in a country in transition: a population based survey in Tirana City, Albania. J Epidemiol Community Health 2003; 57:734-739.

28.Shapo L, McKee M, Coker R, Ylli A. Type 2 diabetes in Tirana City, Albania: a rapid increase in a country in transition. Diabet Med 2004; 21:77-83.

29.Shapo L, Pomerleau J, McKee M. Physical inactivity in a country in transition: a population-based survey in Tirana City, Albania. Scand J Public Health 2004; 32:60-67.

30.Spahija B, Qirjako G, Toçi E, Roshi E, Burazeri G. Socioeconomic and lifestyle determinants of obesity in a transitional southeast European population. Med Arh 2012; 66(3 Suppl 1):16-20.

31.Studimi demografik dhe shwndetesor i Shqipwrise, 2008-2009. Available at: http:/ / www.measuredhs.com/ pubs/ pdf/ FR230/ FR230.pdf. Accessed on February 2013.

32.Kondapalli LA, Molinaro TA, Sammel MD, Dokras A. A decrease in serum estradiol levels after human chorionic gonadotrophin administration predicts significantly lower clinical pregnancy and live birth rates in in vitro fertilization cycles. Hum Reprod 2012; 27 :2690-2697.

33.Al-Ghamdi A, Coskun S, Al-Hassan S, Al-Rejjal R, Awartani K. The correlation between endometrial thickness and outcome of in vitro fertilization and embryo transfer (IVF-ET) outcome. Reprod Biol Endocrinol 2008; 6:37.

34.Lawlor DA, Nelson SM. Effect of age on decisions about the numbers of embryos to transfer in assisted conception: a prospective study. Lancet 2012; 379:521-527.

35.Schieve LA, Peterson HB, Meikle SF, Jeng G, Danel I, Burnett NM, Wilcox LS. Live-birth rates and multiple-birth risk using in vitro fertilization. JAMA 1999; 282:1832-1838.

36.Witsenburg C, Dieben S, Van der Westerlaken L, Verburg H, Naaktgeboren N. Cumulative live birth rates in cohorts of patients treated with in vitro fertilization or intracytoplasmic sperm injection. Fertil Steril 2005; 84:99-107.

37.Olivius K, Friden B, Lundin K, Bergh C. Cumulative probability of live birth after three in vitro fertilization/ intracytoplasmic sperm injection cycles. Fertil Steril 2002; 77:505-510.