Patterns of infertility in Poland – multicenter study

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Abstract

OBJECTIVE: Infertility seems to be a great worldwide problem. Many publications present the epidemiology of infertility, but the percentage distribution of factors responsible for infertility varies significantly. The objective was to define infertility profiles in Poland assessed according to the information provided by 4 large infertility centers: Bialystok, Poznan, Szczecin and Warsaw.

MATERIAL AND METHODS: Multicenter study was performed. Couples with primary infertility, attending one of the four centers in Poland, were asked to fulfill a questionnaire. Overall 1517 questionaires were analysed: Bialystok – 468, Poznan – 325, Szczecin – 341, Warsaw – 383. Only semen analyses fulfilling WHO Manual 1999 criteria were used in the study and were afterwards compared with 2010 WHO standards.

RESULTS: Results from 4 Polish centers showed that the average age of infertile women was 31.41 years and of infertile men 33.2 years. The mean duration of infertility equaled 3.31 years. Among 1517 surveyed women, no pathological findings concerning reproductive abilities were observed in 1088 cases (71.72%). In the remaining patients the following were diagnosed: uterine factor in 26 (6.02%) women, ovulation disorders in 134 (31.33%), including 70 (16.27%) of PCOS patients, tubal factor in 165 (38.55%) and endometriosis in 145 (33.73%). The average of 18.9% of couples had a mixed cause of infertility, while idiopathic factor was assigned to 15.99%. In the study male factor accounted for 55.73% of cases. Change of reference values for semen analysis implemented in 2010 caused an increase in the number of normal results and asthenozoospermia.

CONCLUSIONS: According to the data provided by Polish infertility centers the rate of male factor as a reason of infertility has reached 55.73%. However, the implementation of new reference values for semen analysis in 2010 led to the decrease in male factor frequency and the increase in the rate of idiophatic infertility. Anovulatory cycles and endometriosis are the main reasons affecting the female reproductive potential.

ORIGINAL ARTICLE

INTRODUCTION

Infertility – Epidemiology

According to WHO infertility is defined as a failure to conceive after a year of regular intercourses without contraception. It is mainly due to a low (20%) monthly conceptive abililty of humans. Nowadays around 13–18% of couples of reproductive age are dealing with the problem of conceiving their offspring. Almost 40% of infertility cases are associated with male factor, in Poland it reaches 52% (Semczuk *et al.* 2006; Wolczynski 2006). According to the classic definition, in United States infertility concerns 13–14% of couples among the population from 15 to 44 years of age. In France similar problem concerns 15.8% of couples. According to Danish data the lifetime prevalence of infertility in the studied population was 26.4% (Schmidt 2006).

Ability to conceive decreases with age – slightly after 35, while after 45 giving almost no chance to have the own biological offspring. The reason why a particular woman cannot get pregnant can be defined in 45–65% of patients.

Almost 85% of all couples suffer from subfertility, which is defined as decreased reproductive ability. In 3–5% of infertile couples there is no possibility to be succesfully treated (Aboulghar 2003; Shushan 1995).

Male infertility

At the beginning of this century the male factor of infertility was considered of minor importance. Mostly women were pointed out as those responsible for procreation failure. First elaboration of male factor was published in 1980 when WHO released the first edition of *Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction*. In 1987, 1992, 1999 and 2010 revised editions of the manual were published (WHO 1999; 2010).

In recent decades semen quality diminished. Carlsen *et al.* (1992) asserted that sperm quantity and quality had declined over the previous 50 years. Their paper was a meta-analysis of semen quality from European and American fertility centers, which presented average sperm densities in 1940: 113×10^6 ml and in 1990: 66×10^6 ml. WHO experts changed norms for the reference values of semen (WHO 1999). That may have caused a shift in the pattern of male factor occurrence.

Another change will be observed soon, as in 2010 the newest edition of the WHO manual (2010) was published. WHO 1999 and 2010 lower reference values are presented in Table 1.

Tab. 1. Normal reference values (WHO 1999 and 2010) of human semen.

Parameter	Lower reference limit according to WHO	
	1999	2010
Semen volume (ml)	2–5	1.5 (1.4–1.7)
Total sperm number (10^6 per ejaculate)	–	39 (33–46)
Sperm concentration (10^6 per ml)	20	15 (12–16)
Progressive motility (PR, %)	50	32 (31–34)
Sperm morphology (normal forms, %)	14*	4 (3.0–4.0)
Peroxidase-positive leukocytes (10^6 per ml)	1.0	1.0

*According to Krűger

OBJECTIVE

To define infertility profiles in Poland assessed according to the information provided by 4 large infertility centers: Bialystok, Poznan, Szczecin and Warsaw.

MATERIAL AND METHODS

Multicenter study was performed. Overall 1517 questionnaires were analyzed (Bialystok – 468 <CENTER 1>, Poznan – 325 <CENTER 2>, Szczecin – 341 <CENTER 3>, Warsaw – 383 <CENTER 4>). Infertile couples attending one of the four centers in Poland were asked to fulfill a specially prepared questionnaire. The study was performed in years 2007 thru 2011.

The infertile couples had to fulfill two obligatory inclusion criteria. Only primary infertility was taken into consideration and the duration of infertility had to be at least one year, according to WHO definition.

Based on the questionnaire responses female infertility factor was defined as: uterine, ovarian, tubal, endometriosis or none of the above. Either HSG or laparoscopy was needed for the assessment of tubal factor. Diagnosis of endometriosis was based on laparoscopy with histopathological examination. PCOS was diagnosed on the basis of Rotterdam criteria.

Only semen analyses fulfilling WHO Manual 1999 criteria were used in our study.

To compare the changes that occurred after the introduction of new standards of semen analysis, the pathology of semen was shown using both 1999 and 2010 standards.

Statistical analysis was performed with the use of Statistica 9.0 software, where $p<0.05$ was considered significant.

RESULTS

Age

Results from 4 centers showed that the average women's age was 31.41 and men's – 33.2 years among the population of infertile couples in Poland.

In Center 4 the average women's age was 31.59, men's – 33.74 years. In Center 3 it was 31.12 and 33.56, respectively. The results in Center 2 and 1 were also similar: 31.4 and 31.14 years for female age and 33.31 and 32.83 years for male age, respectively. No statistically significant differences in age of couples (man and woman) were found among the centers taking part in the study.

Duration of infertility

The mean duration of infertility for the couples in Poland was 3.31 years. The average values were as follows: Center 1 – 3.32 years; Center 2 – 3.92 years; Center 3 – 2.49 years; Center 4 – 3.12 years. The differences among Centers were statistically significant (Center 3 vs. Center 2, p=0.0001 and Center 1 vs. Center 4, p=0.0207).

Sperm analysis among Centers

Average values of semen analysis in the studied population are presented in Table 2.

The mean sperm volume for all the men included in the study was 3.08 ml and did not differ significantly among the studied Centers.

The values of sperm count were different in the studied Centers. It ranged from azoospermia to 202 mln/ml, with the mean sperm count of for all the Centers of 44.86 mln/ml. The highest mean sperm count was in Center 1 (53.51 mln/ml), the lowest – in Center 2 (32.84 mln/ml).

The mean rate of type A motility spermatozoa was 12.3% in all Centers. The mean rate of type B motility spermatozoa was 25.4% in all studied Centers. Pathological findings in morphology were found in 61.16% of all the analyzed spermatozoa. The lack of motile spermatozoa and lack of pathology were observed in patients with azoospermia. There were no changes in semen quality with regard to men's age.

According to the division of semen pathology, their types were determined as a percentage using 1999 and 2010 standards. There has been no change in percentage of azoospermia. Taking into account 2010 standards, the percentage of normospermia and asthenozoospermia significantly increased (from 8.46% to 45.92% and from 29.14% to 34.35%, respectively) (Figure 1, Table 3).

Female causes of infertility

Among 1517 surveyed women, no pathological findings concerning reproductive abilities were observed in 1088 cases (71.72%). Among the remaining patients the following were diagnosed: uterine factor in 26 (6.02%) women, ovulation disorders in 134 (31.33%), including 70 (16.27%) of PCOS patients, tubal factor in 165 (38.55%) and endometriosis in 145 (33.73%). In some patients more than one infertility factor was found (Figure 2).

Significant age-dependent differences in the incidence of particular types of female factors among women were observed in the study (Table 4).

In women older than 30 years the rate of tubal factor and endometriosis increased significantly (p<0.05), while ovulation disorders decreased (p<0.05) in comparison to women younger than 30 years of age.

Tab. 2. Analysis of semen in the studied population.

Parameter	Mean	Range	
		Minimum	Maximum
Semen volume (ml)	3.08	0.5	20
Sperm number (mln/ml)	44.86	0.0	202
Type A progressive motility (%)	12.3	0.0	70
Type B progressive motility (%)	25.40	0.0	60
Type C motility (%)	20.29	0.0	68
Type D motility (%)	42.29	0.0	90
Sperm pathology (%)	61.16	0.0	99
Leukocyte number (mln/ml)	0.85	0.2	20.8

Tab. 3. Change in the prevalence of semen pathology depending on applicable standards.

	WHO 1999		WHO 2010	
	n	%	n	%
Normozoospermia	150	8.46	700	45.92
Asthenozoospermia	418	29.14	470	34.35
Asthenoteratozoospermia	462	29.70	81	3.04
Oligoasthenozoospermia	113	6.20	51	4.17
Oligoasthenoteratozoospermia	315	22.18	156	9.11
Azoospermia	59	4.32	59	4.32

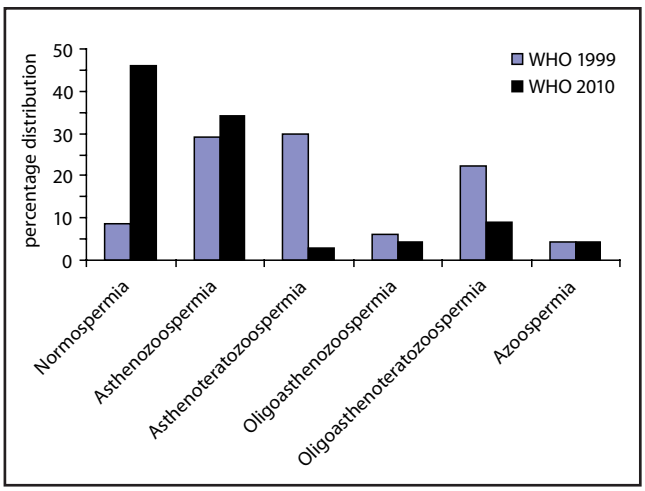

Fig. 1. Change in the prevalence of semen pathology depending on applicable standards

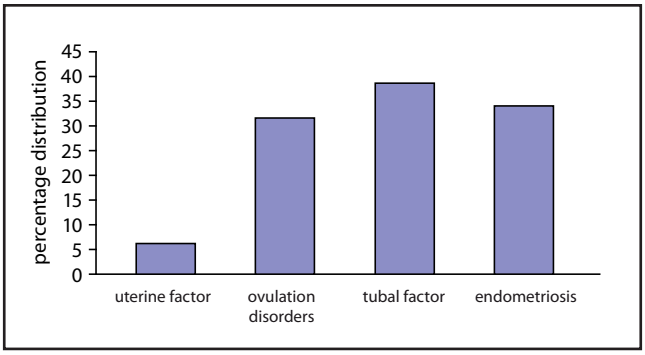

Fig. 2. The prevalence of female infertility factors

Tab. 4. The prevalence of female infertility factors according to age.

Female factor	Up to 30 years of age	> 30 years of age
Uterine factor	4.62%	6.90%
Ovulation disorders (including PCOS)	44.67% (31.91%)	25% (9.48%)
Tubal factor	29.79%	41.38%
Endometriosis	27.66%	37.07%

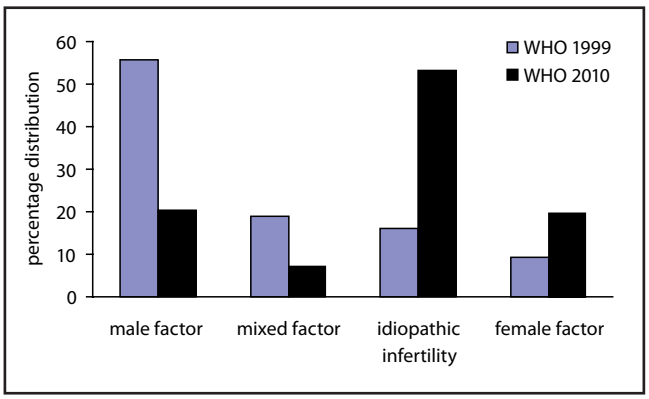

Fig. 3. Change in the prevalence of male and female factors depending on the applicable standards of semen analysis.

Analysis of the pattern of infertility causes

Statistical analysis of the pattern of infertility causes showed the dominating role of male factor in the studied population. Abnormalities were found in 55.73% of all the surveyed men. The highest rate of abnormalities in semen analysis was found in Center 2 (74.51%), the lowest – in Center 3 (44%).

The female factor as the only cause of infertility in the couple was rather rare – 8% (mean rate calculated for all the studied Centers). No such cases (isolated female factor) were found in Center 2, while in Center 4 the prevalence was the highest of all four and reached 13%.

In around 18.9% of couples the reason of infertility was mixed (Center 2 – 25.49%, Center 3 – 15%).

After combining the rates of isolated female factor and mixed factor of infertility, the overall frequency of female abnormalities affecting reproductive ability reached 26.62%.

After summing up the rates of isolated male factor and mixed factor of infertility, the overall frequency of male abnormalities affecting reproductive ability reached 76.7%.

Idiopathic infertility was assigned to 15.99% of all the analyzed population.

The change of reference values for semen analysis implemented in 2010 caused an increase in the number of normal results and asthenozoospermia. It is a result of liberalization of normal values – it shifted some men with oligoasthenoteratozoospermia and oligoasthenozoospermia to normozoospermia and asthenozoospermia groups.

Upon analyzing the same data according to 2010 WHO manual, isolated male factor decreased from 55.73% to 20.34%, while mixed factor decreased from 18.9% to 7%. The new reference values caused an increase of isolated female factor to 19.38% and a great increase in the prevalence of idiopathic infertility factor (from 15.99% to 53.05%) (Figure 3).

DISCUSSION

Infertility is a growing social problem. The main difficulty in the diagnosis and treatment is its complex and multifactorial nature.

The mean age of both men and women attending fertility clinics in 4 Centers in Poland was similar. Recently a slight increase in the average age of couples trying to conceive has been observed. In the above study the average age of women was 31 and of men 33 years of age. The age shift results in an increasing number of patients undergoing diagnosis and treatment of infertility. It must be remembered that the age of the female partner is crucial and it is now quite common to begin workup after 6 months of unprotected intercourse in patients older than 35 years of age. A woman in her mid to late 40s, on the other hand, is unlikely to conceive (Derman & Seifer 2007).

The average time from the first attempts to conceive to attending fertility centers was around 40 months. However, it has to be verified and decreased because of the time that the couple had spent with their outpatient clinic doctors – gynecologists, guiding them finally to specialized centers.

Pattern of infertility factors in Poland show an increase in the rate of male factor (57.80%) and a decrease in female factor (7.72%). However, an increase in mixed factor prevalence was also shown (18.9%).

The cumulative male factor frequency was calculated as 76%, while for female it was 26% (it exceeds 100% as a result of mixed factor analyzed separately). The distribution of female infertility causes in the worldwide literature varies greatly. The percentage of infertile couples due to the tubal factor ranges from 11 to 76.7%. Ovulation disorders relate to 10.9% – 49.1% of infertile patients. Uterine factor can coexist in 3.2–48% of cases (Pisarski & Szamatowicz 1997; Guzick *et al.* 1998; Tehrani *et al.* 2011; Wolczynski 2006; Miller *et al.* 1999). Cahill & Wardle (2002) suggest that ovulatory disorders can be determined in 25% of patients, tubal factor occurs in 20%, endometriosis in 5% of women, while the uterine factor is seen in less than 1% of the respondents. Infertility of unexplained etiology is found in 25% of infertile couples. Derman and Seifer (2007) reported that generally around 40% of human infertility is attributable to female causes, 40% to male causes and 20% to the combination of both. Cahill & Wardle (2002) imply that male factor varies in the range of 30%. According to other authors male factor can be confirmed in 26.2–46.6% of couples, while idiopathic infertility occurs with a frequency of 3.5–22.1% (Pisarski & Szamatowicz 1997).

The most frequently observed change in the quality of semen was asthenozoospermia (from 37.39% to 58.84%). The rate of oligozoospermia was 28.38% according to WHO 1999 reference values. The above prevalence was concise with the data published by El-Migdadi *et al.* (2005). According to their clinical awareness study performed on 287 male patients in the North of Jordan, the rate of oligozoospermia was 31.4%. The rate of azoospermia in the studied material was 4.32% and is lower than previously published by Janczewski *et al.* (1990).

The small number of female patients attending studied fertility clinics may be the result of specific characteristics of Centers included in the study. Additionally, some of the patients with ovulation disorders are successfully treated by their gynecologists and they never reach a specialized center. It is interesting that in Center 2 no woman had an isolated female factor of infertility. However, the treatment of the male factor is performed mainly in large clinics offering andrological care, such as all four studied Centers. That is the reason of such a high prevalence of male factor (according to WHO 1999) in the analyzed group. Those facts leave the opportunity for conclusion that the real frequency of factors of infertility in Poland are different from achieved and presented in this study.

Change of reference values for semen influences the rates of male factor infertility. According to the new WHO normal values the prevalence of male factor will be diminished and unexplained infertility rate will be greatly increased. For more precise analysis of male factor additional functional tests of spermatozoa should be taken into account in the future.

CONCLUSIONS

According to the data provided by Polish infertility centers the rate of male factor as a reason for infertility reached 76.7%, however, the specificity of the above centers may provide biased data: male and idiopathic factor may be overestimated and female factor of infertility – underestimated. The implementation of new reference values for semen analysis in 2010 has led to the decrease in the prevalence of male factor, increase of isolated female factor and great increase in idiopathic infertility. The prevalence of particular female factors seems to be age-related.

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REFERENCES

1 Aboulghar MA, Mansour RT, Serour GI, Al-Inany HG (2003). Diagnosis and management of unexplained infertility: an update. Arch Gynecol Obstet. **267**: 177–88.
2 Cahill DJ, Wardle PG (2002). Management of infertility. BMJ. **325**: 28–32.
3 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE (1992). Evidence for decreasing quality of semen during past 50 years. BMJ. **305**: 609.
4 Derman SG, Seifer DB (2007). Evaluation of female infertility. In: Alvero R, Schlaff WD, editors. Reproductive Endocrinology and Infertility: The Requisites in Obstetrics and Gynecology. Philadelphia: Mosby. p. 155–168.
5 El-Migdadi F, Banihani I, Banihani SA (2005). Clinico-hormonal correlation of oligospermic patients in the below sea level environment (Jordan Valley). Neuro Endocrinol Lett. **26**: 13–8.
6 Guzick DS, Sullivan MW, Adamson GD, Cedars MI, Falk RJ, Peterson EP, Steinkampf MP (1998). Efficacy of treatment for unexplained infertility. Fertil Steril. **70**: 207–13.
7 Janczewski Z, Bablok L, Smith A, Czaplicki M, Fracki S (1990). Male infertility and its treatment: A review of over 4700 patients treated for male related infertility. Int Urol Nephrol. **22**: 161–65.
8 Miller JH, Weinberg RK, Canino NL, Klein NA, Soules MR (1999). The pattern of infertility diagnoses in women of advanced reproductive age. Am J Obstet Gynecol. **181**: 952–7.
9 Pisarski T, Szamatowicz M, editors (1997). Niepłodnosc [Infertility]. Warszawa: PZWL. p. 14–15.
10 Rowe PJ, Comhaire FH (2000). WHO manual for the standardized investigation, diagnosis and management of the infertile male. World Health Organization. Cambridge University Press.
11 Schmidt L (2006). Infertility and assisted reproduction in Denmark. Epidemiology and psychosocial consequences. Dan Med Bull. **53**: 390–417.
12 Semczuk M, Szymanski W, Kuczynski W (2006). Nieplodnosc meska. Ogolne okreslenia pojecia nieplodnosci, epidemiologia, przyczyny [Male infertility. General concepts, epidemiology and causes of infertility]. In: Semczuk M, Kurpisz M, editors. Andrologia. Warszawa: PZWL. p. 353–359.
13 Shushan A, Eisenberg VH, Schenker JG (1995). Subfertility in the era of assisted reproduction: changes and consequences. Fertil Steril. **64**: 459–69.

14 Tehrani FR, Simbar M, Tohidi M, Hosseinpanah F, Azizi F (2011). The prevalence of polycystic ovary syndrome in a community sample of Iranian population: Iranian PCOS prevalence study. Reprod Biol Endocrinol. **9**: 39.
15 WHO laboratory manual for the examination and processing of human semen (2010). World Health Organization: Fifth Edition.
16 Wolczynski S (2006). Diagnostyka i leczenie niepłodności – stymulacja jajeczkowania i zachowawcze leczenie czynnika męskiego [(Diagnosis and treatment of infertility – ovulation induction and male factor conservative treatment) (In Polish with no English abstract)]. Gin po Dypl: 9–12 (Educational volume: Assisted reproductive technologies in infertility treatment).