

The influence of selected environmental factors on the time of natural menopause in women living in the Małopolskie voivodeship

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ABSTRACT: The main objective of the study is to determine which of the chosen environmental factors and selected groups of such factors alter the time of natural menopause in women living in the Małopolska region. Two hundred and thirty two women aged over 40 years were investigated in a cross-sectional survey in Cracow and the surrounding area. Among them 165 women who had undergone natural menopause and had their last bleeding at least 12 months prior to the interview were chosen. To estimate the age at menopause, a retrospective method was used. Univariate and multivariate methods were employed to estimate association of age at natural menopause with factors of interest. Mean age at natural menopause was 50.32 years (SD=3.82). Among biological and socio-economic factors, only the length of the reproductive period ($H=106.07$; $p=0.000$) and the age at the time of the first birth ($R=0.18$; $p=0.020$) turned out to be associated with the age at natural menopause in the studied group. The length of the smoking period ($R=-0.17$; $p=0.031$), the amount ($F=3.25$; $p=0.04$) and frequency of alcohol consumed ($H=6.95$; $p=0.031$) were the environmental factors related to the time of menopause. Women who drank more and smoked over longer period of time were likely to experience menopause earlier than their less drinking and shorter smoked counterparts. Three factors taken together, frequency of smoking, alcoholic intake and the age the tobacco addiction started ($F=3.87$; $p=0.050$), as well as the consumption of strong alcoholic drinks and the early start of tobacco addiction ($F=2.85$; $p=0.026$) were significantly related to the occurrence of natural menopause.

KEY WORDS: natural menopause, environmental factors, cigarette smoking, alcohol intake

Menopause is one of the components of female reproductive involution. The age at which a woman reaches her menopause is determined by genetic, biological and environmental factors. The rise in average life expectancy due to the development of medicine, health-care awareness as well as improvements

in socio-economic conditions more and more frequently turns our attention to health problems of women, which are partly related to menopause. There is evidence in the literature on menopause that environmental conditions may influence the timing of menopause (Cramer et al. 1996; Spandorfer 1996; Cassou et

al. 1997; Nagata et al. 1998; Meschia et al. 2000; Bradbury 2001; Szwed 2001; Parazzini et al. 2006; Kaczmarek 2007; Stachoń 2007; Parente et al. 2008; Pawlińska-Chmara and Szwed 2008; Pakarinen et al. 2010; Przychodni 2010). To fully understand the background of menopause and find out recommendations for the prophylaxis and promotion of healthy women's ageing, it is important to analyse the influence of environmental modifiers on the characteristics of menopause.

The age at which menopause occurs may be an indicator of the health and biological condition of the population as well as a telltale sign of the occurrence of certain conditions such as osteoporosis, genital carcinoma, disorders of the cardiovascular, digestive or excretory system. Considering the above information, the objective of this study is to analyse which of the selected environmental factors affect the age at natural menopause in women living in the Mazowieckie voivodship, Southern Poland

Materials and methods

The empirical basis of this work includes surveys carried out in late 2010/early 2011 in the Małopolskie voivodeship. The research tool used in the study was an anonymous questionnaire created for this study in the Department of Anthropology of the Jagiellonian University. The questionnaire was presented to respondents by the author in the form of a direct interview. Nineteen questions concerning socio-economic data (place of residence and education), lifestyle behaviour (smoking, passive exposure to cigarette smoke and alcohol intake) and reproductive history (age at menarche and menopause, length of the reproductive peri-

od, number of births given by a woman and the occurrence of miscarriages, as well as the age during the first birth) were asked during interview. The post-menopausal status of study women was estimated according to the guidelines of the World Health Organisation (WHO Report 1981, 1996) and included those whose menstrual periods had ceased due to physiological cessation of ovarian activity and had not occurred for the duration of amenorrhoea, i.e. 12 months from the last menstruation. Such cessation of the ovaries' natural activity was defined as natural menopause. Women with both surgical and hormonally controlled menopause were excluded from further analysis. The sample under study consisted of 165 women whose menopause occurred naturally.

Following biological, socio-economic and lifestyle factors known to be related to the age at menopause were taken into consideration: age at menarche, length of the reproductive period, age at first birth and number of births given by a woman and the occurrence of miscarriages, as well as the age during the first birth; place of residence and education level, smoking, passive exposure to cigarette smoke and alcohol intake. The above variables were taken as categorical variables.

A retrospective method was applied to determine age at menopause and descriptive statistics such as the mean and median values of menopausal age were calculated. Both ANOVA and MANOVA were used to test statistical significance of variability in age at natural menopause according to study factors. The multiple regression model (with step-forward procedure) was used to structure and evaluate factors related to timing of menopause. Statistical software StatGraph 5.0 by StatPoint Technologies and

Table 1. Characteristics of study population

Characteristic	n (%)
Place of residence	
Village	27 (16.4)
City/town	138 (83.6)
Education	
Primary	23 (13.9)
Occupational	27 (16.4)
Secondary	78 (47.3)
Higher	31 (18.8)
Smoking	
Smokers	81 (49.1)
Non-smokers	84 (50.9)
Age when smoking started	
Before the age of 20	39 (48.2)
After the age of 20	42 (52.8)
Duration of the smoking period	
Less than 10 years	23 (28.4)
10 to 30 years	27 (33.3)
More than 30 years	31 (38.3)
Intensity of the habit	
Every day, less than 5 cigarettes	13 (16.0)
Every day, more than 5 cigarettes	47 (58.0)
Once a month and less frequently, less than 5 cigarettes	14 (17.3)
Once a month and less frequently, more than 5 cigarettes	7 (8.6)
Alcohol intake	
Drinking	96 (58.2)
Non-drinkers	69 (41.8)
Type of alcohol consumed	
Strong alcohol	40 (41.6)
Weak alcohol	56 (58.4)
Frequency and quantity of alcoholic drinks consumed	
Every day, less than 250 ml	11 (11.4)
Every day, more than 250 ml	10 (10.4)
Once a month and less frequently, less than 250 ml	23 (23.9)
Once a month and less frequently, more than 250 ml	55 (57.3)

Statistica 7.1 by StatSoft were used for calculations.

Results

Biological, demographic, socio-economic and lifestyle characteristics of the study group are shown in Table 1. Mean age of studied women was 64.5 years. Mean age at natural menopause was 50.32 years (SD=3.82) and the median value was 50 years.

The results of the Kruskal-Wallis test showed that among biological factors, only the length of the reproductive period ($H=106.07$; $p=0.000$) was responsible for the variation in the age at natural menopause. The Spearman's rank correlation analysis demonstrated that there was a relationship between the age at natural menopause and the age of the respondent at first birth ($R=0.18$; $p=0.020$). Women who gave birth to her first child later in life, underwent menopause later.

The results of one-way analyses indicate that both the length of the smoking period

($R=-0.17$; $p=0.031$) and alcohol intake ($F=3.25$; $p=0.04$) as well as the frequency of alcohol consumption ($H=6.95$; $p=0.031$) influenced the age at natural menopause. The age at natural menopause in the surveyed group decreased with growing quantity and frequency of alcohol intake as well as an extended smoking period. These dependencies are shown in Figures 1 and 2.

One-way analyses of remaining variables referring to cigarette smoking, such as: fact of smoking ($p=0.148$), number of cigarettes smoked ($p=0.124$), smoking frequency ($p=0.214$) and the age the subject started smoking ($p=0.273$), did not alter the age at natural menopause. Also the variables related to passive exposure to cigarette smoke (passive exposure to cigarette smoke ($p=0.556$), the period of passive exposure to cigarette smoke ($p=0.198$), mean time of exposure to cigarette smoke per day ($p=0.415$), did not reveal significant impact on the age at natural menopause. No effect of alcohol intake ($p=0.182$) or alcohol type ($p=0.102$) was observed in relation to

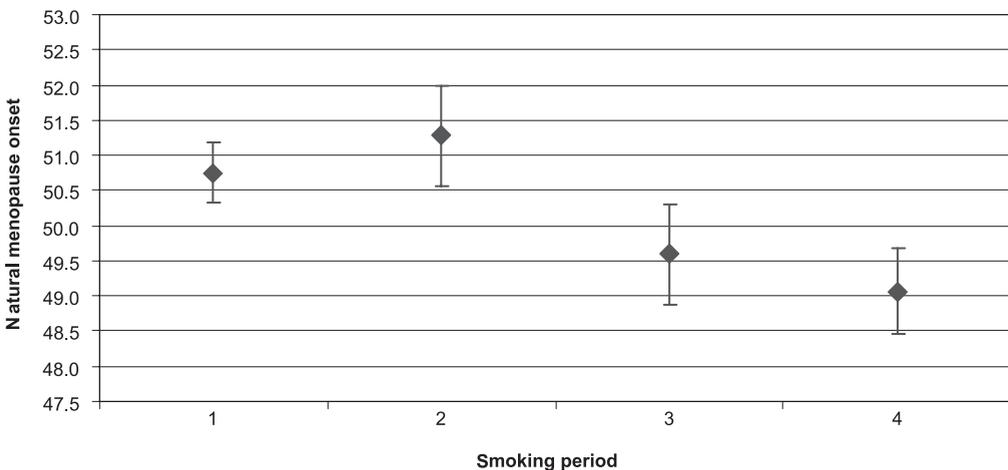


Fig. 1. Timing of natural menopause (mean \pm standard error) in relation to length of cigarette smoking period (where: 1 – non-smokers; 2 – less than 10 years; 3 – 10 to 30 years; 4 – more than 30 years)

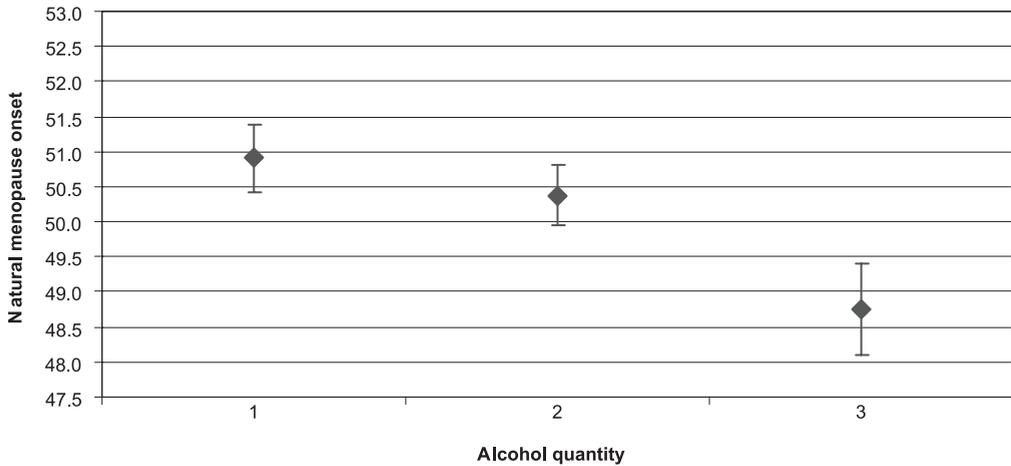


Fig. 2. Timing of natural menopause (mean \pm standard error) in relation to alcohol intake (where: 1 – non-drinkers; 2 – less than 250 ml; 3 – 250 to 700 ml)

age at natural menopause, either. Likewise, socio-economic factors were not related to age at menopause of studied women (education: $p=0.834$; place of residence $p=0.382$).

The results obtained from multivariate analyses confirm the cumulative nature of the investigated factors and point

to differences which could not be identified by means of one-way methods. The quantity of alcohol consumed in combination with smoking frequency were significantly related to age at menopause ($F=5.97$; $p=0.003$). This result shows Figure 3.

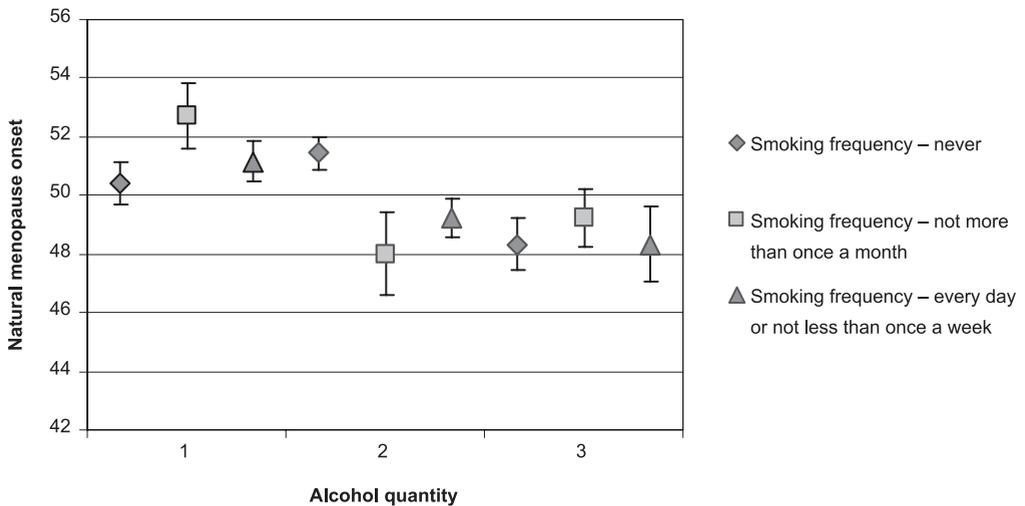


Fig. 3. Timing of natural menopause (mean \pm standard error) in relation to alcohol intake (where: 1 – non-drinkers; 2 – less than 250 ml; 3 – 250 to 700 ml) and smoking frequency

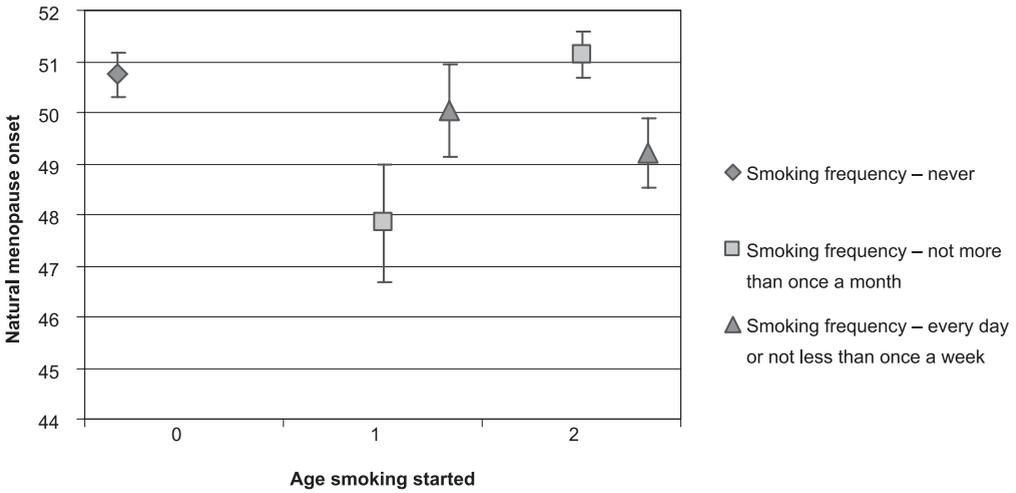


Fig. 4. Timing of natural menopause (mean \pm standard error) in relation to length of smoking frequency and age when the smoking habit started (where: 0 – non-smoker; 1 – before 20 years of age; 2 – after 20 years of age)

Among women who did not drink alcohol, those who smoked frequently were more likely to have menopause earlier than occasionally smoked had, and earlier onset of menopause was typical for non-smokers than for two other groups of women. This may be due to the

impact of additional factors, both biological, such as duration of the menstruation period, as well as environmental considerations, such as diet. Moreover, earlier menopause could have been influenced by genetic factors which were not investigated in the study. In the group of wom-

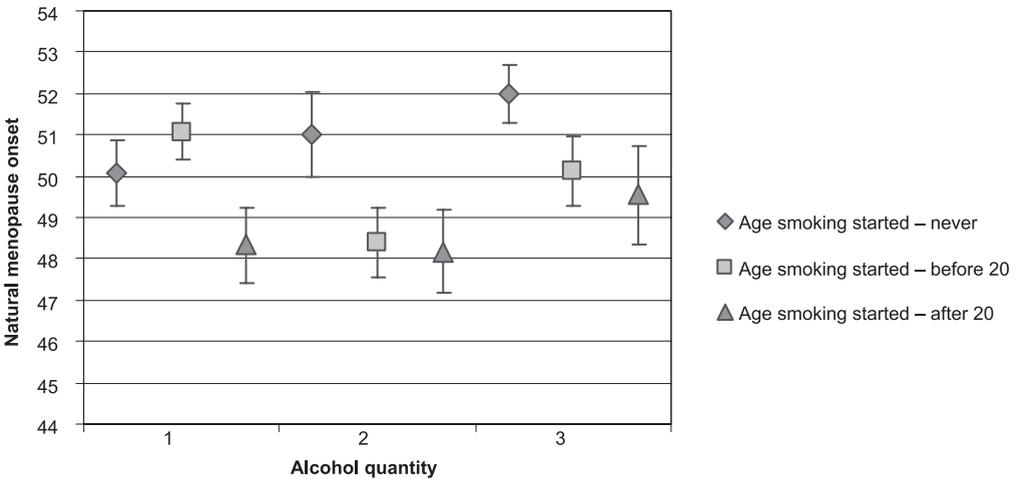


Fig. 5. Timing of natural menopause (mean \pm standard error, 52–59 years) in relation to average daily alcohol intake (where: 1 – non-drinkers; 2 – less than 250 ml; 3 – 250 to 700 ml) and age when the tobacco addiction started

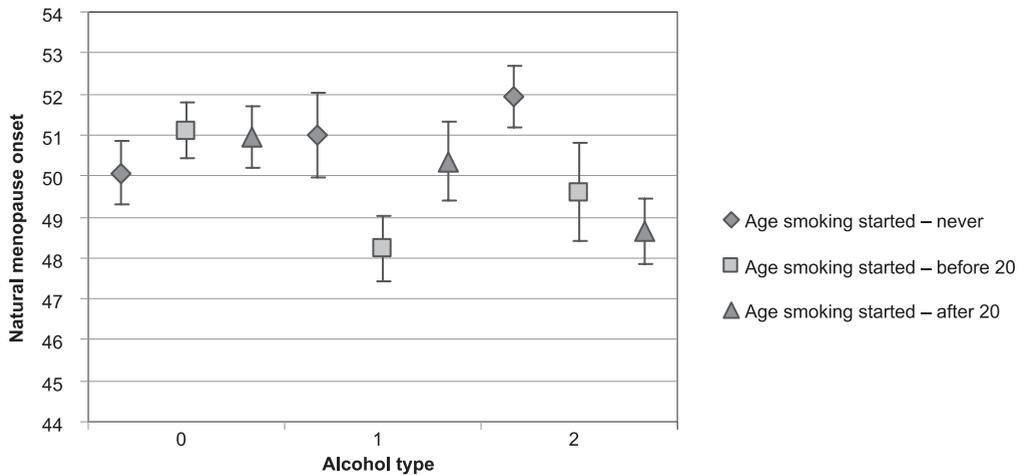


Fig. 6. Timing of natural menopause (mean \pm standard error) in relation to age when the tobacco addiction started and type of alcohol drink (where: 0 – non-drinkers; 1 – strong alcohol drink; 2 – weak alcohol drink)

en who drank small quantities of alcohol – up to 250 ml of alcoholic drink per day on average, and from 250 to 700 ml of alcoholic drink per day – the onset of menopause was later for non-smokers than smokers, quite opposite than observed among non-drinkers. Frequent tobacco use was significantly related to age at menopause also when the age of starting smoking was added ($F=4.41$; $p=0.037$). Women who started smoking before 20 years of age and smoked less frequently were likely to have menopause at younger age. Women whose tobacco addiction started after 20 years of age did not differ in menopausal age, however more frequent smokers were likely to have menopause earlier than their less frequently smoking counterparts (Fig. 4). The age when the smoking habit started was also significantly related to menopausal age ($F=2.60$; $p=0.038$). Women who started smoking after 20 years of age and drank smaller quantities of alcohol (less than 250 ml per day) had their menopause at

a later age than their study counterparts (Fig. 5).

Those women who started smoking before 20 years of age and in addition drank strong alcoholic drinks had menopause at the earliest age of all studied groups. Never smoked women did not reveal variability of menopausal age regardless whether they drank weak or strong alcohol (Fig. 6).

Three-way MANOVA, including age at the start of smoking, smoking frequency and alcohol intake ($F=3.87$; $p=0.050$) did not reveal any relation of these factors to age at menopause. Nor did smoking frequency, age when the tobacco addiction started, type of alcohol consumed, and smoking frequency, type of alcohol consumed, and average alcohol intake per day. Other variables were not subjected to multivariate analysis due to the non-homogeneity of variance.

The multiple regression model (step-forward procedure) showed that the average alcohol intake per day ($t=-$

2.390, $p=0.018$) explained the largest part of variation in menopausal age.

Discussion

In study sample, mean age at natural menopause was 50.32 years (SD=3.82) and median was 50.00 years. This result corroborates well with other studies using the retrospective method such as Rodziewicz-Gruhn (1998) (mean age=49.89), Meschia et al. (2000) (mean age=50.90), Stachoń (2007) (mean age=50.18; median=50.33), Pawlińska-Chmara and Szwed (2008) (mean age=49.81, median=50.00 lat). Different values of mean and median age at natural menopause were reported by Szwed (2001) (mean age=48.57, median=49.00) and Przychodni (2010) (mean age=49.48; median=50.00). These discrepancies may be due to various sampling methods and sample size. According to Kaczmarek (2007), the most common age range at which Polish women experience natural menopause is 45–55 years and median age at menopause for the nation-wide sample is 51.2 years.

In the study sample, the smoking period proved to be related to the age at menopause in a statistically significant way ($R=-0.17$; $p=0.031$). For women who smoked longer (from 10 to 30 years or more than 30 years), the onset of menopause was earlier than for non-smokers or those women who smoked for a shorter period (less than 10 years). Similar results were obtained in a study by Cramer (1996). A reverse relationship, albeit statistically insignificant, was found by Stachoń (2007). There are numerous evidence of the relationship between smoking habit and age at menopause indicating earlier menopausal age of smoking women (Cramer et al.1996; Spandorfer

1996; Nagata et al. 1998; Meschia et al. 2000; Bradbury 2001; Szwed 2001; Parazzini et al. 2007; Kaczmarek 2007; Stachoń 2007; Parente et al. 2008; Pawlińska-Chmara and Szwed 2008; Pakarinen et al. 2010; Przychodni 2010).

Mattison and Thorgeirsson (1978) explained the probable mechanism responsible for early onset of menopause in women who are heavy smokers. They found that benzopyrene, a polycyclic aromatic hydrocarbon contained in cigarette smoke, when inhaled in its gaseous form by laboratory mice, caused the destruction of primary ovarian follicles. Assuming that the same process occurs in women, an earlier occurrence of menopause may be expected even in those women who gave up smoking many years before the onset of menopause. According to the mechanism suggested by Mattison and Thorgeirsson, the more tobacco is smoked by a woman in her life, the more egg cells are damaged, hence the earlier the onset of menopause in comparison to women who have never smoked. Other research proved a relationship between exposure to multinuclear hydrocarbons contained in cigarettes and increase in the induction of the pro-apoptotic BAX protein in the ovaries (Bradbury 2001). Tests on laboratory animals suggest that the nicotine contained in cigarettes blocks aromatase, an enzyme responsible for converting androgens to oestrogens in such locations as the granular cells of the ovarian follicles (McLean et al. 1977 cited in Parente et al. 2008). Moreover, the toxicity of substances contained in cigarettes was observed with reference to liver enzymes which control the circulation of oestrogens in blood (Johansson et al. 1996). Nevertheless, not all studies confirm the effect of smoking on the age at natural menopause (Carda et

al. 1998; Parazzini 2007). The ambiguity of the results may have been caused by a small sample size and the impact of other factors which were not included in the above analysis. As smoking is perceived negatively by society, especially with reference to women, the possibility of understating the number of cigarettes smoked or denying the tobacco addiction by the respondents must also be taken into account.

Alcohol intake was another factor under analysis. Among the variables characterising this factor, both frequency use ($H=-6.95$; $p=0.031$) and the average intake of alcohol consumed per day ($F=3.25$; $p=0.04$) were significantly related to age at menopause. A tendency for an earlier onset of natural menopause can be noticed in relation to increased alcohol intake as well as the frequency of alcohol consumption. Numerous tests on animals confirm the effect of alcohol on the reproductive system (van Thiel et al. 1978). Studies by van Thiel et al. (1978) demonstrated that ovarian failure in female rats who were fed for 7 days with alcohol in the quantity equivalent to 36% of their daily energetic requirement was more frequent than in the group which was not fed with alcohol. Findings presented by van Emanuele et al. (2002) indicate that rats which were fed with small amounts of alcohol had an increased level of estradiol in their blood. Sarkola et al. (2001) noticed a short-term surge in blood testosterone level in rats which consumed alcohol. Since testosterone has an inhibitory effect on the hypothalamus as well as the pituitary gland. An increase in its level may disrupt the menstrual cycle. Tests carried out by Gavalier and Rosenblum (1987) on rats which had had their ovaries surgically removed (simulating

a post-menopause state) confirmed that alcohol intake (4.4 g alcohol/1 kg of body mass/day for 10 weeks) resulted in an increase in the level of oestrogen in those animals. Similar results, both in the case of small and medium doses of alcohol, were reported in studies on women by Mendelson and Mello (1988), Gavalier, van Thiel (1992) and Dorgan et al. (2001). Studies by Johannes et al. (1997) proved that the estradiol level in women who consumed large quantities of alcohol was lower than in those who did not drink alcohol at all. Pakarinen et al. (2010) also provided evidence for relationship between alcohol intake and the onset of menopause. According to these findings, menopause appears earlier in women who drink alcohol than in those who abstain from drinking, although this is true only for alcohol consumed within a maximum of one week before the test. A study by Kaczmarek (2007) does not reveal any relationship between alcohol intake and the age at natural menopause, whereas results presented by Kinney et al. (2006) suggest the existence of a reverse tendency. Definitive determination of the effect of alcohol intake on the age at natural menopause in women is problematic, since there are no long-term randomised tests concerning this subject, and retrospective surveys are encumbered with errors due to the fallibility of the human memory. A tendency to understate the quantity and frequency of alcohol intake by women also needs to be taken into consideration. Subjects who drink alcohol may also differ from non-drinkers by other characteristics not included in the above analyses.

In this work, the impact of socio-economic status on the age at natural menopause was also studied. Many authors state that women of higher socio-eco-

conomic status (measured by the level of education) are characterised by a later timing of menopause (Cassou et al. 1997; Kaczmarek 2007; Parazzini et al. 2007). The present work analysed, among other factors, place of residence and education and their relation to age at natural menopause. None of these two factors were related to menopause. The findings are in line with those obtained by Carda et al. (1998); Meschia et al. (2000); Stachoń (2007) and Przychodni (2010).

Results of multivariate analysis of variance (MANOVA) provided information on the interdependence between selected environmental factors and age at natural menopause. It was established that of all studied lifestyle factors, smoking frequency, age when smoking started and the quantity of alcohol consumed interact with one another affecting age at which natural menopause occurred ($F=3.87$; $p=0.05$). Moreover, by means of multivariate analysis it was possible to indicate relation of the type of alcohol consumed to menopausal age. Women who drank strong alcoholic drinks (vodka, cognac) and who started smoking before they were 20 had their menopause earlier in comparison to women who drank weaker alcohol or were non-drinking respondents. On the other hand, women who drank strong alcoholic drinks but whose tobacco addiction started after they were 20, had their menopause later than respondents who smoked their first cigarette before they were 20. Interestingly, women who drank small intake of alcohol (less than 250 ml per day) had their menopause at a later age than their counterparts. Similar results concerning the effect of the alcohol intake on the age at natural menopause were obtained in other studies (Emanuele et al. 2002; Register et al. 2002). The influence of

the number of cigarettes smoked on the age at natural menopause was found by McKinlay et al. (1985) and Kinney et al. (2008, cited in Parente et al. 2008) and Szwed (2001). According to these findings, menopause occurred earlier for women who smoked more cigarettes per day. Cramer et al. (1996) also found that age at which the tobacco addiction starts is significant for the timing of natural menopause. Menopause in women who started smoking before 20 years of age commonly occurred earlier than for the subjects whose smoking habit started later on.

Finally, thanks to the use of the multiple regression method, it was possible to indicate a factor which was responsible for the characteristics of natural menopause to the greatest extent. The step-forward method ranked the average alcohol intake per day as the factor explaining the largest portion of variation in menopausal age. Unfortunately, few publications discuss the effect of this factor on age at natural menopause. The present work also revealed that the impact of this factor may be modified by other concurrent factors, which as yet have not been described, either. Note that the age at which menopause occurs is determined not only by environmental or biological, but also by genetic factors. The age at which women menopause depends on quantitative characteristics, the variability of which has its root causes in various genotypes and reaction norms. They act in a complex way yielding a unique result as demonstrated by the individual profiles of menopause.

Conclusions

The extended smoking period and high alcohol intake (above 250 ml per day) can

increase risk of an earlier timing of natural menopause. The influence of environmental factors on age at menopause is of a complex nature. Age at which women started smoking in combination with the frequency and the quantity of alcohol intake were related to age at natural menopause. Consumption of strong alcoholic drinks such as vodka, cognac, whisky, in combination with an earlier start of cigarette smoking (before age 20) were related to earlier timing of menopause. The factor which had the most pronounced effect on the age at natural menopause was the average alcohol intake per day. Alcohol intake of no more than 250 ml of alcoholic drink per day was associated with a later onset of natural menopause, while greater quantities resulted in an earlier occurrence of menopause. However, given the small sample size, objective measurement of environmental factors influence on age at natural menopause needs to be performed in large population studies in order to confirm current findings concerning menopausal timing.

Authors' contribution

ESz conceived the concept, designed and performed the research project, performed statistical analysis, interpreted data and drafted the manuscript; KSz supervised the research project and verified statistical outcomes. Both authors read and approved the final manuscript.

Conflicting interests

The authors declare that they have no conflicts of interest in the research.

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