Original Article

Secular Trend of Menopausal Age and Related Factors among Tehrani Women Born from 1930 to 1960; Tehran Lipid and Glucose Study

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Abstract

Background: Menopause is an important milestone of a woman's reproductive life. There is limited data on the secular trend of menopausal age. The purpose of this study is to identify the secular trend of menopausal age and its related factors among Tehrani women born during 1930 – 1960.

Methods: A total number of 2266 women, born between 1930and 1960, were recruited among TLGS participants. The World Health Organization classification was used to define menopause status. Birth cohorts were created using 10-year periods, and statistical comparisons were performed with analysis of covariance (ANCOVA).

Results: The means for menopausal age of women born in the 1930s, 1940s and 1950s were 48.5, 49.5 and 49.9 years, respectively. After adjustment for possible confounding factors in the linear regression model, the increasing trend of menopausal age was constant (P = 0.029).

Conclusion: There is an increasing trend in menopausal age in female residents of Tehran. These findings have implications for endogenous lifetime exposure of women to gonadal steroids.

Keyword: Menopausal age, trend, secular trend, Tehran Lipid and Glucose Study (TLGS)

Introduction

Menopause is defined as the permanent cessation of ovarian activity which constitutes part of normal aging.[1] The end of women's reproductive life with implications for their socio-psychological status and body health is an important event in a woman's lifetime.[2] The median age of onset was estimated to be between 48 and 52 years but varies from 40 to 60 years[3,4]; its timing is influenced by various factors such as genetics, lifestyle, BMI, reproductive and hormonal status.[5–7]

Age at menopause can be predictive of health and diseases status; early or late menopause can make women susceptible to several chronic diseases. Studies have shown that older age at menopause increases the risk of breast and endometrial cancer,[8,9] whereas early menopause has been associated with risk of cardiovascular diseases, osteoporosis and all-cause mortality.[10–12] Understanding the variability and determinants of menopausal age may help with the development of new strategies to improve women's health and their quality of life.

Limited studies have addressed the secular trend and determinants of menopausal age.[13–15] Although some studies have reported that age at menopause does not change through time,[16] according to recent studies, age at menopause seems to be shifting toward higher ages in various countries.[2,14] In Finland, the medians of menopausal age were 50 and 51 years in 1997 and in 2007, respectively.[17] In Gothenburg, the increasing trend was 0.1 year per birth year in women born between 1908 and 1930.[13] Although factors such as smoking and parity have been found to affect the timing of menopause, the evidence is relatively inconclusive.[18–22]

Knowledge regarding trend in age at menopause in Iranian women is limited because of the small number of longitudinal studies documented on premenopausal women.[13] Furthermore, the role of genetic and environmental factors restricts generalization of results from studies in other countries to Iranian populations. The purpose of this study was to identify the secular trend of menopausal age and the role of certain socio-demographic, anthropometric and reproductive factors in age at menopause among Tehrani women, born during 1930–1960.

Materials and Methods

The participants of the present study were selected from among TLGS participants, an ongoing prospective study being conducted to determine the prevalence and risk factors for non-communicable diseases among a representative population of Tehran; sampling methods have been described in details elsewhere; briefly, this study began in 1999 and its data is being collected and assessed every 3 years.[23–25]At baseline, 15005 Tehrani residents,

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Table 1. Characteristics of women according to their birth decade.

	1940's	1950's	1960's
Age[*]	81.2 ± 3.5	72.2 ± 3.7	61.7 ± 4.2
Menopausal age[*]	48.5 ± 5.9	49.5 ± 6.09	49.9 ± 3.6
BMI[*]	27.2 ± 4.5	28.9 ± 4.5	29.9 ± 4.5
Parity[*]	5.7 ± 2.6	5.3 ± 2.3	4.2 ± 1.8
Literacy[•]			
Illiterate	72.1	43.1	14.7
Low	25.5	49.7	64.6
High	2.4	7.1	20.7
Ever smoking[•]			
Yes	10.1	5.9	5.6
No	89.9	94.1	94.4
[*]The continuous variables are described as Mean ± SD; [•]The categorized variables are described as Percentage			

Table 2. Variables identified by stepwise regression analysis as predictors of menopausal age.

Model	Beta	95% CI	*P*-value
Birth decade	0.05	0.03, 0.7	0.029
Smoking status	-0.05	-1.92, -0.26	0.01
Education	0.07	0.25, 0.92	0.001

aged ≥3 years were included; there were 5615 female participants born between 1930 and1960. We excluded women who were pregnant, those who had undergone hysterectomy and/or oophorectomy (uni/bilateral) prior to their reported menopausal age, and those who had not experienced menopause (n = 3349). Written informed consent was obtained from the 2266 women who met the inclusion criteria. The ethical committee of Research Institute for Endocrine Sciences approved this study. The variables evaluated were educational level, number of parity, smoking and passive smoking, body mass index (BMI), waist circumference (WC) and waist to hip ratio (WHR).

Natural menopause was determined as defined by the World Health Organization: absence of spontaneous menstrual bleeding for more than 12 months, for which no other pathologic or physiologic cause could be determined. Since the month of menopause was not asked, we assumed that all respondents experienced their menopause at the midpoint of the year reported.

Education was categorized into three levels: illiterate, low (primary and secondary), and high (diploma and higher degrees). Parity was also categorized in three groups; 0–3, 4–6 and ≥7 pregnancies. The participants' BMI was divided into three groups: <25, 25–29, and ≥30 (Kg/m^2). Smoking status was categorized as never or ever smokers and passive smoking, i.e., any history of exposure to environmental tobacco smoke at work and/or at home as "positive" and no history of exposure as "negative".

There is a positive correlation between BMI and estradiol level,[26] suggesting an association between age at menopause and anthropometric parameters. Anthropometric measurements included height and weight, for which we used values measured in the TLGS; weight was measured with the women minimally clothed, without shoes, using a digital scale and recorded to the nearest 100 grams, and height was measured in a standing position, without shoes, using a tape measure, while the shoulders were in a normal position. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters (kg/m^2).

Statistical analysis

Data, stratified by decades of birth are presented at 10-year intervals. Results for continuous variables are given as means (±SD) and for categorical variables as percentages. Analysis of covariance (ANCOVA) was used to compare the data presented at 10 years intervals. Linear regression analysis (stepwise method) was done with adjustment for possible confounding factors, including educational level, number of parity, smoking status, passive smoking, BMI, WC and WHR. Statistical analyses were performed using SPSS for windows version 15 and *P*-values <0.05 were considered statistically significant.

Results

The mean age and age at menopause of participants were 58.1 ± 7.9 and 49.6 ± 4.8 years, respectively. All statistical analyses were performed based on women's birth decades. Approximately 70% of women born between 1930 and 1940 were illiterate, while half of the women born during the 1940s had low levels of education and 64.5% of women born between 1951 and 1960 had medium or higher levels of education. The means of menopausal age in women born in the 1930s, 1940s and 1950s were 48.5, 49.5 and 49.9 years, respectively. According to our findings, the age range of menopause in 47.2% of cases was 47–52 years; mean body mass index (BMI) was 29.15 ± 4.63 Kg/m^2. Table 1 summarizes the characteristics of women according to their birth decade.

There was an increasing trend of one-year per decade among women born in the 1930s and 1940s and an increasing trend of 0.4-year per decade in women born in the1940s and 1950s.

After adjustment for possible confounding factors such as BMI, education, number of parity, and smoking in the linear regression model, the increasing trend of menopausal age was 0.05 year per decade increase in birth year. Our results showed that smoking had a significant negative, and levels of education had significant positive effects on menopausal age (Table 2).

Significant results from one-way analysis of variance (ANOVA) followed by *post-hoc t*-tests showed a significant difference between means of menopausal age of women born in the 1930s compared to those born in the1940s and 1950s (*P* = 0.042, *P* < 001, respectively), but there was no significant difference between women born in the1940s and 1950s (*P* = 0.11). Confidence intervals were overlapping in three decades (Figure 1).

Table 3 shows the multivariate model and the factors affecting menopausal age including birth decade, smoking, passive smoking, parity, BMI, education, waist and WHR; education and smoking.
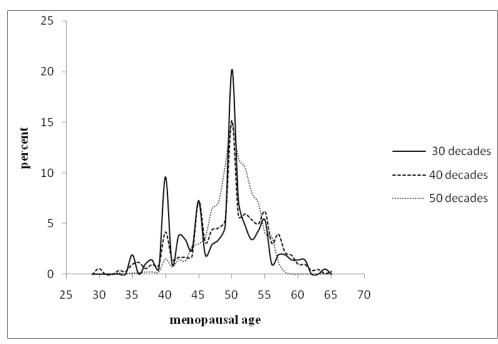
Figure 1. Relative frequency of menopausal age during three decades in TLGS sample.

Table 3. Analysis of covariance explaining menopausal age by covariates (Birth decade, Education, Smoking, Passive smoking, Parity, Body Mass Index, Waist Circumferences, Waist/Hip Ratio).

Covariates	β	95% CI	*P*-Value
Birth decade			
1930's	-0.73	-1.57, -0.11	0.08
1940's	-0.25	-0.75, 0.25	0.32
1950's	0 (Reference)		
Smoking status			
No	1.02	0.10, 1.94	0.02
Yes	0 (Reference)		
Passive smoking			
No	0.23	-0.27, 0.74	0.37
Yes	0 (Reference)		
Parity			
≤3	-0.45	-1.14, 0.23	0.19
4–6	-0.11	-0.7, 0.48	0.71
≥ 7	0 (Reference)		
BMI(Kg/m2)			
<25	-0.82	-1.71, 0.06	0.06
25–29	-0.32	-0.93, 0.29	0.3
>29	0 (Reference)		
Education			
Illiterate	-1.25	-2.02, -0.47	0.002
Low	-0.08	-0.74, 0.57	0.79
High	0 (Reference)		
WC(cm)	-0.03	-0.07, 0.005	0.09
WHR	4.16	0.02, 8.3	0.04

Discussion

According to this study, the means of menopausal age in women born in the 1930s, 1940s, and 1950s were 48.5, 49.5 and 49.9 years, respectively. There was a significant increasing trend of 1year per decade for women born in the 1930s and 1940s and a non-significant increasing trend of 0.4year per decade among those born in the 1940s and 1950s. We found a secular trend in age at menopause in three decades, a trend which remained significant even after adjustment for confounding factors including

BMI, WC, WHR, education, number of parity, smoking status and passive smoking.

The presence of a secular trend is controversial,[14] with recent studies showing a significant change in mean age at menopause over time. Our findings are in agreement with some previous studies. Pakarinen et al., found that the menopausal age increased one year in Finland during 1997–2007.[17]In a survey of over 1400 Swedish women born between 1908 and 1930, Rodstrom et al., (2003) found a progressive and significant increase in the mean ages at natural menopause, i.e., 48.5 years for those born in 1908

and 51 years for those born in 1930.[13] Similar results were reported by Nichols et al., (2006) for 22,774 American women born between 1910 and 1969; the mean age at natural menopause increased from 49.1 years for those born in 1915–1919 to 50.5 years for those born in 1935–1939.[27] However, these results were not supported by others, i.e., researchers who studied a population-based random sample of 7828 white women and found no evidence of a secular trend towards a later age at menopause in the last 25 years.[16] In 1996, McKinlay, in an overview of population based studies, reported that there was no evidence of any secular trend in age at menopause.[28]

We assume this increase in menopausal age is related to lifestyle changes during recent years.[29] Previously some studies have observed that overweight or obese women may experience menopause at a later age.[30] Moreover, some researchers suggested that lower education be associated with an earlier age at menopause.[31,32] Since this study has revealed an increase in both BMI and education among women born in three various decades, we assumed that this increase in menopausal age may result from lifestyle changes.

It is assumed that some confounding variables including sociodemographic, anthropometric and reproductive factors can affect the age at menopause. According to our results, an inverse relationship was found between the age at menopause and smoking status; women who smoked cigarettes were more likely to experience earlier menopause, while passive smoking was not significantly associated with early menopause. This finding adds to recent evidence documented by previous studies which claim an independent association between smoking and early menopause.[33–36] Similar to Mikkelsen et al., and Cooper et al.[19,35] we found no association between passive exposure to smoking and early menopause. There are various hypotheses for the biological mechanism of smoking that leads to earlier menopause; it has long been suggested that tobacco smoke contains polycyclic hydrocarbons which may affect ovarian germ cells and lead to follicular exhaustion and a lower level of blood estrogen.[33,34]

We found a significant association between educational level and age at menopause, as women with a higher level of education experienced menopause later than those with lower levels, consistent with reports of some previous studies that found low educational status to be a risk factor for early menopause.[37,38] However, one study reported that higher education was associated with lower age at menopause.[39] On the other hand, some authors believe that there is no link between educational status and age at menopause.[40–42] Level of education is one of the socioeconomic factors which may influence the menopausal age through effects on the pattern and quality of diet, parity, physical activity and BMI but the precise nature of these relationships is unclear.

We observed that age at menopause did not vary with parity and the trend remained constant after adjustment in agreement with Brambilla and Okonofua's findings.[43,44] Some other investigators, however, observed a trend of increasing age at menopause with an increasing number of live births.[18,45]

Although we observed no significant association between BMI and age at menopause, the menopausal age of women with BMI <25 occurred 0.8 years earlier in comparison to obese women. Similarly, others[39,46] have reported that BMI has a statistically significant impact on age at menopause, and in patients with high BMI, menopause tended to occurs at a later age; these findings are in contrast with two recent researches.[47,48]

Our study has certain limitations. The reliability of self-reported ages of natural menopause has been questioned. Available evidence suggests that, because of errors in recall and visible digit preference (specifically the use of zero and five as terminal digits),[27] the use of self reported age at menopause may result in an underestimation of the true mean age at menopause. Additionally in our cohort study, we have just analyzed three available groups of women born during the years 1930 to 1960. Also, uncontrolled confounding that affects menopausal age may produce biased results. Despite these possible limitations, there are certain important aspects of the design of this population study that may have enhanced the possibility of accurately analyzing the trend in menopausal age. We also had a population-based random sample, which increases the generalizability of the results. Questions were exactly the same throughout the study years, which increases the comparability and the quality of the findings, as well.

Our study shows that there is a secular trend in menopausal age. We know that with increase in age at menopause, the risk of breast and endometrial cancer increases. Also, with the increase in life expectancy, women nowadays spend one third of their life time after menopause.[49] Identifying the secular trend of menopausal age can help health policymakers to predict the best age for screening common diseases in this period to consequently improve health and quality of life.

Acknowledgments

References

1. National Institutes of Health State-of-the-Science Conference statement: management of menopause-related symptoms. *Ann Intern Med.* 2005; **142:** 1003 – 1013.
2. Dratva J, Gomez Real F, Schindler C, Ackermann-Liebrich U, Gerbase MW, Probst-Hensch NM, et al. Is age at menopause increasing across Europe? Results on age at menopause and determinants from two population-based studies. *Menopause.* 2009; **16:** 385 – 394.
3. Sowers MR, La Pietra MT. Menopause: its epidemiology and potential association with chronic diseases. *Epidemiol Rev.* 1995; **17:** 287 – 302.
4. Tehrani FR, Solaymani-Dodaran M, Tohidi M, Gohari MR, Azizi F. Modeling age at menopause using serum concentration of anti-mullerian hormone. *J Clin Endocrinol Metab.* 2013; **98:** 729 – 735.
5. Gold EB, Sternfeld B, Kelsey JL, Brown C, Mouton C, Reame N,et al. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40–55 years of age. *Am J Epidemiol.* 2000; **152:** 463 – 473.
6. Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. *Obstet Gynecol.* 1994; **84:** 29 – 34.
7. Farahmand M, Tehrani FR, Pourrajabi L, Najafi M, Azizi F. Factors associated with menopausal age in Iranian women: Tehran Lipid and Glucose Study. *J Obstet Gynaecol Res.* 2013; **39:** 836 – 841.
8. McPherson CP, Sellers TA, Potter JD, Bostick RM, Folsom AR: Reproductive factors and risk of endometrial cancer. The Iowa Women's Health Study. *Am J Epidemiol.* 1996; **143:** 1195 – 1202.
9. Colditz GA. Epidemiology of breast cancer. Findings from the nurses' health study. *Cancer.* 1993; **71:** 1480 – 1489.
10. Atsma F, Bartelink ML, Grobbee DE, van der Schouw YT. Postmenopausal status and early menopause as independent risk factors for cardiovascular disease: a meta-analysis. *Menopause.* 2006, **13:** 265 – 279.
11. Kritz-Silverstein D, Barrett-Connor E, Hollenbach KA: Pregnancy

and lactation as determinants of bone mineral density in postmenopausal women. *Am J Epidemiol.* 1992; **136:** 1052 – 1059.

12. Jacobsen BK, Heuch I, Kvale G. Age at natural menopause and all-cause mortality: a 37-year follow-up of 19,731 Norwegian women. *Am J Epidemiol.* 2003; **157:** 923 – 929.

13. Rodstrom K, Bengtsson C, Milsom I, Lissner L, Sundh V, Bjourkelund C. Evidence for a secular trend in menopausal age: a population study of women in Gothenburg. *Menopause.* 2003; **10:** 538 – 543.

14. McKinlay SM, Bifano NL, McKinlay JB: Smoking and age at menopause in women. *Ann Intern Med.* 1985; **103:** 350 – 356.

15. Danubio ME, Sanna E. Secular changes in human biological variables in Western countries: an updated review and synthesis. *J Anthropol Sci.* 2008; **86:** 91 – 112.

16. Pakarinen M, Raitanen J, Kaaja R, Luoto R. Secular trend in the menopausal age in Finland 1997-2007 and correlation with socioeconomic, reproductive and lifestyle factors. *Maturitas.* 2010; **66:** 417 – 422.

17. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, Skurnick J. Factors associated with age at natural menopause in a multiethnic sample of midlife women. *Am J Epidemiol.* 2001; **153:** 865 – 874.

18. Cooper GS, Sandler DP, Bohlig M: Active and passive smoking and the occurrence of natural menopause. *Epidemiology* 1999; **10:** 771 – 773.

19. Meschia M, Pansini F, Modena AB, de Aloysio D, Gambacciani M, Parazzini F, et al. Determinants of age at menopause in Italy: results from a large cross-sectional study. ICARUS Study Group. Italian Climacteric Research Group Study. *Maturitas.* 2000; **34:** 119 – 125.

20. Nagel G, Altenburg HP, Nieters A, Boffetta P, Linseisen J. Reproductive and dietary determinants of the age at menopause in EPIC-Heidelberg. *Maturitas.* 2005; **52:** 337 – 347.

21. Lawlor DA, Ebrahim S, Smith GD. The association of socio-economic position across the life course and age at menopause: the British Women's Heart and Health Study. *BJOG* 2003; **110:** 1078 – 1087.

22. Ramezani Tehrani F, Moslehi N, Asghari G, Gholami R, Mirmiran P, Azizi F. Intake of dairy products, calcium, magnesium, and phosphorus in childhood and age at menarche in the tehran lipid and glucose study. *PLoS One.* 2013; **8:** e57696.

23. Zarkesh M, Faam B, Daneshpour MS, Azizi F, Hedayati M: The relationship between metabolic syndrome, cardiometabolic risk factors and inflammatory markers in a Tehranian population: the Tehran lipid and glucose study. *Intern Med.* 2012; **51:** 3329 – 3335.

24. Barzin M, Hosseinpanah F, Malboosbaf R, Hajsheikholeslami F, Azizi F. Isolated post-challenge hyperglycaemia and risk of cardiovascular events: Tehran Lipid and Glucose Study. *Diab Vasc Dis Res.* 2013; **10:** 324 – 329.

25. Nichols HB, Trentham-Dietz A, Hampton JM, Titus-Ernstoff L, Egan KM, Willett WC, Newcomb PA. From menarche to menopause: trends among US Women born from 1912 to 1969. *Am J Epidemiol.* 2006; **164:** 1003 – 1011.

26. McKinlay SM. The normal menopause transition: an overview. *Maturitas.* 1996; **23:** 137 – 145.

27. Age of Menarche and its Relationship with Some Factors in the Schoolgirls of Gorgan in 2006. *Journal Of Gorgan Bouyeh Faculty Of Nursing & Midwifery.* 2010; **7:** 48 – 54.

28. Tehrani FR, Mirmiran P, Zahedi-Asl S, Nakhoda K, Azizi F. Menarcheal age of mothers and daughters: Tehran lipid and glucose study. *East Mediterr Health J.* 2010; **16:** 391 – 395.

29. Do KA, Treloar SA, Pandeya N, Purdie D, Green AC, Heath AC, et al. Predictive factors of age at menopause in a large Australian twin study. *Hum Biol.* 1998; **70:** 1073 – 1091.

30. Dorjgochoo T, Kallianpur A, Gao YT, Cai H, Yang G, Li H, et al. Dietary and lifestyle predictors of age at natural menopause and reproductive span in the Shanghai Women's Health Study. *Menopause.* 2008; **15:** 924 – 933.

31. Hayatbakhsh MR, Clavarino A, Williams GM, Sina M, Najman JM. Cigarette smoking and age of menopause: a large prospective study. *Maturitas.* 2012; **72:** 346 – 352.

32. Parente RC, Faerstein E, Celeste RK, Werneck GL. The relationship between smoking and age at the menopause: A systematic review. *Maturitas.* 2008; **61:** 287 – 298.

33. Mikkelsen TF, Graff-Iversen S, Sundby J, Bjertness E. Early menopause, association with tobacco smoking, coffee consumption and other lifestyle factors: a cross-sectional study. *BMC Public Health.* 2007; **7:** 149.

34. Fleming LE, Levis S, LeBlanc WG, Dietz NA, Arheart KL, Wilkinson JD, et al: Earlier age at menopause, work, and tobacco smoke exposure. *Menopause.* 2008, **15:** 1103 – 1108.

35. Castelo-Branco C, Blumel JE, Chedraui P, Calle A, Bocanera R, Depiano E, et al. Age at menopause in Latin America. *Menopause.* 2006; **13:** 706 – 712.

36. Luborsky JL, Meyer P, Sowers MF, Gold EB, Santoro N. Premature menopause in a multi-ethnic population study of the menopause transition. *Hum Reprod.* 2003; **18:** 199 – 206.

37. Parazzini F. Determinants of age at menopause in women attending menopause clinics in Italy. *Maturitas.* 2007; **56:** 280 – 287.

38. Brand PC, Lehert PH. A new way of looking at environmental variables that may affect the age at menopause. *Maturitas* 1978; **1:** 121 – 132.

39. Neslihan Carda S, Bilge SA, Öztürk TN, Oya G, Ece O, Hamiyet B: The menopausal age, related factors and climacteric symptoms in Turkish women. *Maturitas.* 1998; **30:** 37 – 40.

40. Kato I, Toniolo P, Akhmedkhanov A, Koenig KL, Shore R, Zeleniuch-Jacquotte A: Prospective study of factors influencing the onset of natural menopause. *J Clin Epidemiol.* 1998; **51:** 1271 – 1276.

41. Brambilla DJ, McKinlay SM: A prospective study of factors affecting age at menopause. *J Clin Epidemiol.* 1989; **42:** 1031 – 1039.

42. Okonofua FE, Lawal A, Bamgbose JK. Features of menopause and menopausal age in Nigerian women. *Int J Gynaecol Obstet.* 1990; **31:** 341 – 345.

43. te Velde ER, Dorland M, Broekmans FJ. Age at menopause as a marker of reproductive ageing. *Maturitas.* 1998; **30:** 119 – 125.

44. Morris DH, Jones ME, Schoemaker MJ, McFadden E, Ashworth A, Swerdlow AJ. Body mass index, exercise, and other lifestyle factors in relation to age at natural menopause: analyses from the breakthrough generations study. *Am J Epidemiol .*2012; **175:** 998 – 1005.

45. Hardy R, Kuh D, Wadsworth M. Smoking, body mass index, socioeconomic status and the menopausal transition in a British national cohort. *Int J Epidemiol* 2000; **29:** 845 – 851.

46. Amigoni S, Morelli P, Chatenoud L, Parazzini F. Cross-sectional study of determinants of menopausal age and hormone replacement therapy use in Italian women. *Climacteric.* 2000; **3:** 25 – 32.

47. Abedzadeh Kalarhoudi M, Taebi M, Sadat Z, Saberi F. Assessment of quality of life in menopausal periods: a population study in kashan, iran. *Iran Red Crescent Med J.* 2011; **13:** 811 – 817.