British Journal of Medicine & Medical Research
4(35): 5678-5688, 2014

SCIENCEDOMAIN *international*
www.sciencedomain.org

Putative Risk Factors among Ghanaian Women Presenting with Leiomyoma

H. S. Opare-Addo[1], W. K. B. A. Owiredu[2], T. Dapilah[2*] and A. Alhassan[3]

[1]Department of Obstetrics and Gynecology, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
[2]Department of Molecular Medicine, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
[3]Department of Human Biology, School of Medicine and Health Science, University for Development Studies, Ghana.

Authors' contributions

This work was carried out in collaboration between all authors. Authors HSOA, WKBAO and TD conceived and designed the study, wrote the protocol, and performed the statistical analysis. Authors HSOA, TD and AA wrote the first draft of the manuscript. Authors TD and AA managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

Received 5th June 2014
Accepted 30th July 2014
Published 16th August 2014

ABSTRACT

Aims: The objective of the current study was to investigate potential demographic, lifestyle, and medical history risk factors for leiomyoma in a sample of Ghanaian women.
Study Design: A case-control study was conducted among women who attended the Gynecology department of Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana.
Place and Duration of Study: The study took place between May 2005 and March 2009 at the Obstetrics and Gynecology Department of the Komfo Anokye Teaching Hospital (KATH), Kumasi.
Methodology: Premenopausal Ghanaian women aged 20-40 years were studied for the role of putative socio-demographic, lifestyle, and medical history risk factors in the development of leiomyoma. Two hundred women with confirmed uterine fibroids and two hundred women with no observable fibroids were recruited as controls for the study.
Results: Family history (OR 2.21, 95% CI:2.21-5.9) and obesity (OR 3.60, 95% CI:1.74-7.47), nulliparity (OR6.5, 95%CI:4.18-10.0), age at first birth (OR 2.82, 95%CI:1.60-4.98), induced abortion (OR 3.33, 95%CI:1.11-9.99), and history of sexually transmitted

**Corresponding author: Email: tdapilah@yahoo.com;*

infections (OR 2.27, 95%CI:1.21-4.28), all greatly increased the risk of fibroids, not married (OR1.62, 95%CI:1.07-2.44), alcohol intake (OR1.69, 95%CI:1.13-2.53), and contraceptive use (OR1.66, 95%CI:1.11-2.46) also significantly increased the risk of fibroids.

Conclusion: The results of this study describe the association of fibroids with specific lifestyle and medical history risk factors. The present study also revealed that past induced abortions is a significant risk factors for the development of leiomyoma among Ghanaian women.

Keywords: Leiomyoma; fibroids; risk factor; Ghana; women.

1. INTRODUCTION

Uterine fibroid (UF) or leiomyoma is a common benign tumor of the uterine smooth muscle. Most of the hysterectomies done in hospitals are due to the condition [1,2]. Similarly uterine fibroids account for 40% of all major gynecological surgeries in Ghana [3]. The results of several studies have estimated that 30–70% of women who have fibroids are in their premenopausal years [4,5]. Symptoms of uterine fibroids include pelvic pain, low back pain, irritable bowel, heavy menstrual bleeding and even premature labor and infertility [2,6,7]. Uterine fibroids are rarely associated with mortality but they can cause significantly increased health care costs and negative health experiences [6-11]. Several research results have suggested that uterine fibroids represent a hormone dependent disease [7,10,11]. Research conducted in most developed countries have established risk factors that include age, African-American lineage, early age of menarche and nulliparity [6,10]. Studies suggest that African-American women have 2–3 times the risk of uterine fibroids than Caucasian women [4,12] even though there were no significant ethnic differences in hormone levels and other known risks [5,6,12]. In comparison with Caucasian women, African-American women have a higher prevalence of hypertension, diabetes and obesity [6,13], which are independent risk factors associated with uterine fibroids.

In general, previous studies evaluating risk factors for leiomyoma have included only populations based in developed countries. However there are several factors such as diet, exercise, culture, health seeking behavior that are quite different from the ones that pertain in the developing countries such as Ghana. The current study investigated the natural history of leiomyoma among women in Ghana, a developing country, with one of the highest prevalence of the condition. Fibroids accounted for 40% of all gynecological surgeries making it one of the highest in Africa [14]. The objective of the current study was to investigate potential demographic, lifestyle, and medical history risk factors for leiomyoma in a case-control sample of Ghanaian women.

2. METHODOLOGY

A case-control study was conducted among women who attended the Gynecology department of Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana, between May 2005 and March 2009, to determine the risk factors for uterine fibroid. Two hundred (200) women with confirmed uterine fibroids and two hundred other women with no uterine fibroids were recruited as controls for the study a day or two before the planned surgical treatments for them. Both groups were premenopausal women between the ages of 20 and 40 years who were all examined by gynecologists and had transabdominal ultrasound scan also

conducted to confirm their categorization before recruitment. Women with obvious hormonal imbalance, chronic, or malignant diseases were excluded. Details on the study protocol were approved by the Committee on human research and publication (CHRP) of the School of Medical Sciences/KATH.

All subjects consented to participate in the study and completed a structured questionnaire that elicited information on socio-demographic characteristics, tobacco and alcohol consumption, economic background, physical activity, family, medical, previous obstetrics and gynecological histories.

Weight, height, waist circumference and hip circumference were measured by trained staff of the hospital. Weight was measured in the upright position to the nearest 0.1kg using calibrated balance scale. Height was measured without shoes to the nearest 0.1cm using a Gullick II Tape Measure (model 67020) which was mounted on a wall. Body mass index (BMI) was calculated by dividing observed weight by height squared (kg/m2). Waist circumference (WC) was measured to the nearest 0.1cm at the narrowest point between lower end of the rib cage and iliac crest. Hip circumference was measured to the nearest 0.1 cm at the greatest horizontal circumference below the iliac crest at the level of greater trochanter. Waist-to-hip ratio was then computed.

The total weight of tumors removed after surgery were measured and recorded.

2.1 Statistical Analysis

Descriptive statistics for all variables were calculated. Continuous variables were compared using the t-test for independent groups and expressed as means±standard error of mean (SEM). Parameters that were independently related to fibroids were evaluated using univariate logistic regressions. All analyses were two-tailed and P-value<0.05 was considered statistically significant. All statistical analysis were done using Graph Pad Prism version 5.00 for Windows (Graph Pad Software, San Diego California USA, www.grphpad.com).

3. RESULTS AND DISCUSSION

3.1 Socio-dermographic Features

(Table 1) compares the socio-demographic and obstetric/gynecologic features between the patients and the control group. The ages of both patients and control subjects ranged from 20 to 40 years. The results showed a significant difference between the patients and the control subjects when analyzed based on income, education, marital status, alcohol consumption, and familial history of fibroids.

There was a significant positive correlation (r^2=0.9964, p=0.0018) between the age of the patient and the tumor size as shown in (Fig. 1).

There was a significant association with the level of education and the development of fibroids. Those who had secondary and tertiary education were at a more than two fold (OR=2.35, 95% CI=1.33-4.14) and three fold (OR=3.28, 95% CI=1.64-6.55) increased risk respectively of developing fibroids. Those with no education however had a lower risk (OR=0.43, 95% CI=0.26-0.73) associated with fibroid development as shown in (Table 2).

Table 1. Comparison of some demographic and gynecologic characteristics between controls and patients

Variable	Controls	Patients	p value
Age (years)	33.47±0.39	34.62±0.34	0.0288
Income (Ghana Cedi)	85.25±7.18	149.50±6.01	0.0001
Age at menarche (years)	13.38±0.10	12.98±0.09	0.3041
Age at first pregnancy (years)	20.07±0.45	21.13±0.70	0.1987
Age at first birth (years)	23.40±0.90	27.90±0.59	0.0005
Parity	3.00±0.32	1.00±0.32	0.0021
Number of previous abortions	0.83±0.12	1.97±0.13	0.0001
Age at first abortion (years)	18.80±0.23	18.19±0.09	0.0099
Length of menstrual cycle (days)	28.06±0.13	28.24±0.10	0.2740

The data are expressed as Mean±SEM

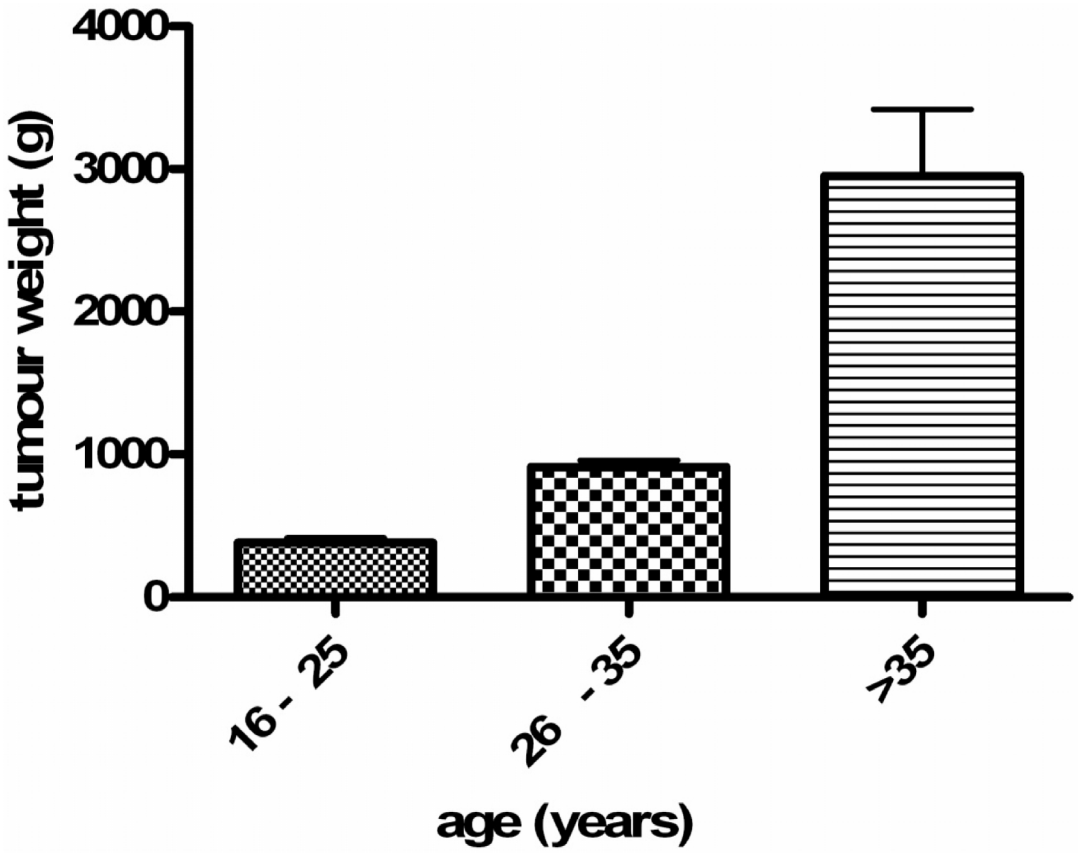

Fig. 1. Correlation between age and the weight of tumor developed

Analysis of the data revealed that there was a significant association between marriage and the development of fibroids (Table 2). Those who had never been married were at a higher risk of developing fibroids compared to those who had ever married (OR=1.62, 95% CI, 1.07-2.44).

Table 2. Frequency distribution and odd ratios for the association of putative risk factors for fibroid development

Parameter	Controls no. (%)	Patients no. (%)	OR	CI
BMI				
Under weight	32(16.0)	18(9.0)	0.70	0.34-1.42
Normal*	64(32.0)	46(23.0)	1.00	
Over weight	54(27.0)	74(37.0)	1.91	1.14-3.20
Obese	26 (13.0)	42(21.0)	2.25	1.21-4.17
W/H ratio				
Obese	13(6.5)	45(22.5)	3.60	1.74-7.47
Normal*	52(26.0)	50(25.0)	1.00	
Education				
No education	88(44.0)	35(17.5)	0.43	0.26-0.73
Basic education*	71(36.0)	65(32.5)	1.00	
Secondary education	27(13.0)	58(29.0)	2.35	1.33-4.14
Tertiary education	14(7.0)	42(21.0)	3.28	1.64-6.55
Marital status				
Ever married*	139(69.5)	117(58.5))	1.00	
Never married	61(30.5)	83(41.5)	1.62	1.07-2.44
Alcohol intake				
Never drank*	132(66.0)	107(53.5)	1.00	
Ever drank	68(34.0)	93(46.5)	1.69	1.13-2.53
Family history of fibroids				
Yes	74(37.0)	28(14.0)	3.61	2.21-5.90
No/not aware*	126(63.0)	172(86.0)	1.00	

**Reference category. OR–Odds Ratio; CI–Confidence Interval; No. –Number of subjects*

Although alcohol intake was common in both controls and patients, the drinkers had a significantly increased risk (OR=1.69, 95% CI=1.13-2.53) of developing fibroids compared to the non-drinkers (Table 2).

Familial history of fibroids in subjects was strongly associated with the development of fibroids as people with such family history were at an increased risk (OR=3.61, 95% CI=2.21-5.90) of developing fibroids compared to people who had no family history of fibroids (Table 2).

3.2 Obstetrics and Gyenaecologic Findings

There was a significant difference between the two groups when data on age at first birth was analyzed (Table 3). The analysis revealed that those who had their first birth at 25 years or more had an increased risk of developing fibroid compared to those who had their first birth before the age of 25 years (OR=2.82, 95% CI=1.60-4.98).

The nulliparous women had an increased risk of developing fibroid compared to those who had one or more live births (OR=6.50, 95% CI=4.18-10.10) as seen in (Table 3).

There was a strong association between history of abortion and the development of fibroid (Table 3). Women who have ever had at least one abortion in the past were at an increased risk of developing fibroid compared to women who had no history of past abortions

(OR=3.35, exact 95% CI=1.90-5.91). Those who had had past induced abortions were also at an increased risk of developing fibroid compared to those who had had spontaneous abortions (OR= 3.33, exact 95% CI=1.11-9.99). Analysis revealed a significant association between the risk for developing fibroid and the use of contraceptives and phytotherapeutic agents. Those who have had past sexually transmitted infections had a higher risk of developing fibroids compared to those who have never had (OR=2.27, exact 95% CI=1.21 - 4.28).

Table 3. Frequency distribution and odd ratios for the association of putative risk factors for fibroid development

Parameters	Controls no. (%)	Patients no. (%)	OR	95% CI
Age at menarche (years)				
≤12	78(39.0)	84(42.0)	1.13	0.76-1.69
>12*	122(61.0)	116(58.0)	1.00	
Age at first birth (years)				
<25*	52(26.0)	50(25.0)	1.00	
≥25	88(44.0)	30(15.0)	2.82	1.60-4.98
Parity				
Nulliparous	46(23.0)	132(66.0)	6.50	4.18-10.10
≥1Births*	154(77.0)	68(34.0)	1.00	
Abortions				
Ever aborted	19(9.5)	52(26.0)	3.35	1.90-5.91
Never aborted*	181(90.5)	148(74.0)	1.00	
Type of abortion				
Spontaneous*	10(5.0)	13(6.5)	1.00	
Induced	9(5.0)	39(19.5)	3.33	1.11-9.99
Age at first abortion (years)				
≤18*	6(3.0)	31(15.5)		
>18	16(8.0)	21(10.5)	3.94	1.32-11.71
Method of delivery				
Ever had a caesarian section	33(16.5)	13(6.5)	0.87	0.42-1.78
Never had a caesarian section*	121(60.5)	55(27.5)	1.00	
Length of menstrual cycle (days)				
≤26	5(2.5)	3(1.5)	0.58	0.14-2.47
27-29*	183(91.5)	189(94.5)	1.00	
≥30	12(6.0)	8(4.0)	0.65	0.26-1.62
Contraception				
Never used*	108(54.0)	83(41.5)	1.00	
Ever used	92(46.0)	117(58.5)	1.66	1.11-2.46
Sexually transmitted infections				
Never infected*	184(92.0)	167(83.5)	1.00	
Ever infected	16(8.0)	33(16.5)	2.27	1.21-4.28
Phytotherapeutic agents				
Never used*	86(43.0)	62(31.0)	1.00	
Ever used	114(57.0)	138(69.0)	1.68	1.11-2.53

**Reference category. OR–Odds Ratio; CI–Confidence Interval; No. –Number of subjects*

3.3 Anthropometric Features

(Table 4) shows the anthropometric features of both patients and controls.

Table 4. Anthropometric features of patients and controls

Parameter	Control	Patients	p value
Weight (Kg)	83.55±3.57	92.50±2.22	0.0326
Height (m)	1.59±0.01	1.60±0.01	0.7060
WC (cm)	66.44±3.31	87.44±3.47	0.0001
HC (cm)	76.79±5.23	92.55±3.91	0.0474
BMI (Kgm^{-2})	22.40±0.22	25.35±0.49	0.0001
WHR	0.87±0.01	0.91±0.01	0.0084
WC/HC	56.30±2.56	49.36±2.06	0.0449

WC: Waist Circumference, HC: Hip Circumference, BMI: Body Mass Index, WHR: Waist-to-Hip Ratio. The data are expressed as Mean±SEM

Weight, waist circumference, hip circumference, BMI, and WHR differed significantly between patients and control subjects.

(Table 5) shows the correlation between the various anthropometric parameters measured in both patients and control subjects. The tumor weight and the BMI had a significant correlation. When subjects were classified as underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9) and obese (≥30), there was a strong association between the development of fibroid and an increase in the patients BMI; with the overweight patients having an almost two fold increased risk (OR=1.91; 95%CI=1.14-3.20) and the obese having far more than a two-fold risk increase (OR=2.25; 95%CI=1.21-4.17) of developing fibroid when compared to the patients with normal BMI. The underweight patients however had a decreased risk (OR=0.70; 95%CI=0.34-1.42) of developing fibroid when compared to the normal BMI patients.

Table 5. Correlation between anthropometric variables for controls (lower left-hand side) and patients (upper right-hand side)

	Weight	height	WC	HC	BMI	WHR	TW
Weight		0.49***	0.53***	0.53***	0.97***	0.14	-0.20
Height	0.47*		0.17	0.15	0.25	0.14	0.15
WC	0.96***	0.43		0.99***	0.53***	0.29*	-0.01
HC	0.96***	0.42	0.89***		0.53***	0.14	0.01
BMI	0.96***	0.22	0.93***	0.93***		0.13	0.04*
WHR	-0.05	-0.05	0.16	-0.29	-0.04		0.03*

**Correlation is significant at the 0.05 level (2-tailed), **correlation is significant at the 0.01 level (2-tailed), ***correlation is significant at the level of 0.001 (2-tailed). WC: Waist Circumference, HC: Hip Circumference, BMI: Body Mass Index, WHR: Waist-to-Hip Ratio*

When subjects were categorized as normal or obese based on their waist-to-hip ratio, there was a strong association between obesity and the development of fibroid (OR=3.60; 95% CI=1.74-7.47) with the obese having an increased risk of developing fibroids.

The findings of the present study indicates that leiomyoma mostly occur among women in their late reproductive ages which is consistent with other research findings [15-17]. This

observations is attributed to the increase risk in new fibroid development and the increased growth of, or increased symptoms from, already existing fibroids, as well as from a greater willingness of women in the later reproductive years to have gynecologic care [7].

This study observed a significant difference in the level of education between the two groups. This study also revealed that those women with tertiary and secondary education had more than a three-fold and two fold risk of developing fibroid compared to women with basic education. The results of this study are consistent with the findings of another study [18]. Highly educated women in Ghana tend to be sedentary, but one of the modifiable risk factors that have been reported for hormonally mediated tumors such as fibroids and breast cancer is physical activity [19,20]. The demands of long years of education means highly educated women tend to defer birth and since parity is protective in the development of leiomyoma [21,22] it may explain the significant difference between the two groups in terms of education.

Unmarried women are more likely to have multiple partners and hence higher risk of contracting STIs. STIs are link to fibroid development. Unmarried women are also more likely to be nulliparous, which is a risk factor for the development of fibroids.

Alcohol plays a variety of roles in Ghanaian culture [23] and so women, particularly the elderly, indulge freely and frequently in the act of alcohol consumption as they go through their daily activities. The findings of this study are consistent with those which also showed that the risk of uterine leiomyoma correlated positively with the years of alcohol consumption and with current consumption of alcohol [24]. Alcohol consumption is associated with higher endogenous levels of oestradiol and estrone which may promote growth of uterine leiomyoma [25-27].

Although the number of previous abortions was considerably high among patients compared to the control subjects. In the present study there was an increase risk of leiomyoma among women who had had previous induced abortions. The mechanism underlining this association is poorly understood but the theory of tissue injury and post abortion infections could be implicated. Abortion procedures and post abortion infections may lead to cellular injury and inflammation which has been proposed as mechanism for the initiation of myoma [2]. In Ghana it is estimated that more than a third of all gynecological admissions are abortion related [28-30]. In many of these cases there are poor post abortion care leading to several complications that could precipitate the development of fibroid.

The study also revealed a higher risk of developing fibroid in women who have had previous sexually transmitted infections (STIs) compared to those who have never had an STI. One a similar study reported a correlation between pelvic inflammatory disease (PID) and leiomyoma [31]. The effect of infectious agents on myometrial tissue has been proposed to explain this observation because of the increasing evidence relating infectious agents to several neoplasms [32], and more specifically because of the observed development of smooth muscle neoplasms among children infected with human immunodeficiency virus [33]. The association of fibroid with chlamydial infection, a common cause of PID further lends credence to this theory [34].

Most of the women used injectable contraceptives whiles a few used oral contraceptives and intrauterine devices (IUD). These injectable contraceptives were mostly progestin-only injectables.

Some studies on the use of steroid contraceptives and hormone replacement therapy have clearly identified the procarcinogenic and anticarcinogenic properties of oestrogens and progestins, respectively, in the endometrium [35].

Overall, it was observed that an increase in body mass index (BMI), weight, and waist-to-hip ratio were each associated with an increase in uterine leiomyoma risk. WHR and BMI also had significant association with tumor weight at surgery in the present study. Other studies have also found similar trends in the different populations [36]. Literature is inconclusive with regards to the role of BMI in the development of leiomyoma. Some studies [12,16,37] have found that the risk of uterine leiomyoma increases monotonically with increasing BMI. Studies in premenopausal women have consistently documented an inverse association between BMI and circulating levels of sex hormone-binding globulin [38-40]. Decreases in sex hormone-binding globulin may increase the amount of free oestrogen or the fraction available for biologic activity [38]. Obesity is associated with decreased 2-hydroxylation of estrone to catechol oestrogens and increased 16-alpha-hydroxylation of estrone to estriol, thereby producing oestrogens with greater uterotropic activity [36,41].

4. CONCLUSION

The results of this present study describe associations of uterine fibroids with specific lifestyle and medical history risk factors. Family history of leiomyoma predisposes women to developing leiomyoma. This study has also shown that among Ghanaian women a history of previous abortion and age at previous abortion also predisposes them to leiomyoma. As revealed in this study increase BMI, WHR and nulliparity are the most independent risk factors for uterine fibroid or leiomyoma among Ghanaian women.

CONSENT

All authors declare that written informed consent was obtained from all subjects before they were enrolled for this study.

ETHICAL APPROVAL

Ethical clearance was obtained from the Committee on Human Research, Publications and Ethics (CHRPE) of the Komfo Anokye Teaching Hospital and the School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. Thus the study was conducted based on the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990-1997. Obstet Gynecol. 2002;99(2):229-34.
2. Stewart EA. Uterine fibroids. Lancet. 2001;357(9252):293-8.
3. Seffah JD. Re-laparotomy after cesarean section. Int J Gynaecol Obstet. 2005;88(3):253-7.

4. Baird DD, et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol. 2003;188(1):100-7.
5. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2008;22(4):571-88.
6. He Y, et al. The association between subclinical atherosclerosis and uterine fibroids. PLoS One. 2013;8(2):e57089.
7. Parker WH. Etiology, symptomatology, and diagnosis of uterine myomas. Fertil Steril. 2007;87(4):725-36.
8. Downes E, et al. The burden of uterine fibroids in five European countries. Eur J Obstet Gynecol Reprod Biol. 2010;152(1):96-102.
9. Williams VS, et al. Uterine fibroids: A review of health-related quality of life assessment. J Womens Health (Larchmt). 2006;15(7):818-29.
10. Flake GP, Andersen J, Dixon D. Etiology and pathogenesis of uterine leiomyomas: A review. Environ Health Perspect. 2003;111(8):1037-54.
11. Walker CL, Stewart EA. Uterine fibroids: The elephant in the room. Science. 2005;308(5728):1589-92.
12. Marshall LM, et al. Risk of uterine leiomyomata among premenopausal women in relation to body size and cigarette smoking. Epidemiology. 1998;9(5):511-7.
13. Zeigler-Johnson CM, et al. Subclinical atherosclerosis in relation to hysterectomy status in black women. Stroke. 1998;29(4):759-64.
14. Seffah JD, Adanu RMK. Hysterectomy for uterine fibroids in nullipara at Korle Bu Teaching Hospital, Ghana. Tropical Journal of Obstetrics and Gynecology. 2005;22.
15. Marshall LM, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol. 1997;90(6):967-73.
16. Ross RK,et al. Risk factors for uterine fibroids: Reduced risk associated with oral contraceptives. Br Med J (Clin Res Ed). 1986;293(6543):359-62.
17. Velebil P, et al. Rate of hospitalization for gynecologic disorders among reproductive-age women in the United States. Obstet Gynecol. 1995;86(5):764-9.
18. Chiaffarino F, et al. Diet and uterine myomas. Obstet Gynecol. 1999;94(3):395-8.
19. Lee IM. Physical activity and cancer prevention--data from epidemiologic studies. Med Sci Sports Exerc. 2003;35(11):1823-7.
20. Matthews CE, et al. Physical activity and risk of endometrial cancer: A report from the Shanghai endometrial cancer study. Cancer Epidemiol Biomarkers Prev. 2005;14(4):779-85.
21. Parazzini F. Risk factors for clinically diagnosed uterine fibroids in women around menopause. Maturitas. 2006;55(2):174-9.
22. Chen CR, et al. Risk factors for uterine fibroids among women undergoing tubal sterilization. Am J Epidemiol. 2001;153(1):20-6.
23. Akyeampong E. Alcoholism in Ghana--a socio-cultural exploration. Cult Med Psychiatry. 1995;19(2):261-80.
24. Wise LA, et al. Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's Health Study. Hum Reprod. 2004;19(8):1746-54.
25. Andersen TI. Genetic heterogeneity in breast cancer susceptibility. Acta Oncol. 1996;35(4):407-10.
26. Reichman ME, et al. Effects of alcohol consumption on plasma and urinary hormone concentrations in premenopausal women. J Natl Cancer Inst. 1993;85(9):722-7.
27. Hankinson SE, et al. A prospective study of reproductive factors and risk of epithelial ovarian cancer. Cancer. 1995;76(2):284-90.
28. Ahiadeke C. Incidence of Induced Abortion in Southern Ghana. International Family Planning Perspectives. 2001;27(2):96-108.

29. Lamptey P. Abortion experience among obstetric patients at Korle-Bu Hospital, Accra, Ghana. Journal of Biosocial Science. 1985;17(2):195-203.
30. Ampofo DA. 330 cases of abortion treated at Korle-Bu Hospital: The epidemiological and medical characteristics. Ghana Medical Journal. 1970;9(3):156-162.
31. Wyshak G, et al. Lower prevalence of benign diseases of the breast and benign tumours of the reproductive system among former college athletes compared to non-athletes. Br J Cancer. 1986;54(5):841-5.
32. Tomatis L, Bartsch H. The contribution of experimental studies to risk assessment of carcinogenic agents in humans. Exp Pathol. 1990;40(4):251-66.
33. McClain KL, et al. Association of Epstein-Barr virus with leiomyosarcomas in children with AIDS. N Engl J Med. 1995;332(1):12-8.
34. Benson RC, Pernoll ML. Benson and Pemoll's Handbook of Obstetrics and Gynecology, ed. R. Benson. New York: McGraw-Hill; 1994.
35. Cook LS, Weiss NS. eds. Endometrial cancer. In: Women and health., ed. M.B. Goldman and M.C. Hatch. Academic Press: London, United Kingdom. 1999;916–31.
36. Schneider J, et al. Effects of obesity on estradiol metabolism: Decreased formation of nonuterotropic metabolites. J Clin Endocrinol Metab. 1983;56(5):973-8.
37. Lumbiganon P, et al. Protective effect of depot-medroxyprogesterone acetate on surgically treated uterine leiomyomas: a multicentre case--control study. Br J Obstet Gynaecol. 1996;103(9):909-14.
38. Dorgan JF, et al. The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women (Maryland, United States). Cancer Causes Control. 1994;5(1):53-60.
39. Verkasalo PK, et al. Circulating levels of sex hormones and their relation to risk factors for breast cancer: A cross-sectional study in 1092 pre- and postmenopausal women (United Kingdom). Cancer Causes Control. 2001;12(1):47-59.
40. Grenman S, et al. Sex steroid, gonadotropin, cortisol, and prolactin levels in healthy, massively obese women: correlation with abdominal fat cell size and effect of weight reduction. J Clin Endocrinol Metab. 1986;63(6):1257-61.
41. Fishman J, Boyar RM, Hellman L. Influence of body weight on estradiol metabolism in young women. J Clin Endocrinol Metab. 1975;41(5):989-91.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=616&id=12&aid=5768