FACTORS ASSOCIATED WITH THE DEVELOPMENT OF HYPERTENSION AMONG SURGICAL MENOPAUSE WOMEN AT HOSPITAL UNIVERSITI SAINS MALAYSIA

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ABBREVIATION

TAHBSO : TOTAL ABDOMINAL HYSTERECTOMY WITH BILATERAL SALPHINGO-OPHERECTOMY

BSO : BILATERAL SALPHINGO-OPHERECTOMY

BMI : BODY MASS INDEX

HRT : HORMON REPLACEMENT THERAPY

DM : DIABETES MELLITUS

CVS : CARDIOVASCULAR DISEASE

LH : LUTEINISING HORMONE

FSH : FOLLICULAR STIMULATING HORMONE

WHO : WORLD HEALTH ORGANIZATION

BP : BLOOD PRESSURE

SBP : SYSTOLIC BLOOD PRESSURE

DBP : DIASTOLIC BLOOD PRESSURE

CRF : CLINICAL RESEARCH FORM

ABSTRAK (VERSI BAHASA MELAYU)

FAKTOR-FAKTOR YANG MEMPENGARUHI HIPERTENSI DI KALANGAN WANITA MENOPOS SELEPAS PEMBEDAHAN DI HOSPITAL UNIVERSITI SAINS MALAYSIA

Pengenalan:

Menopos selepas pembedahan seperti pembuangan rahim dan kedua-dua ovari yang menyebabkan ketiadaan period secara mengejut. Ia menyebabkan risiko untuk mendapat hipertensi mendadak naik sama seperti kaum lelaki, dengan itu risiko untuk dapat penyakit jantung pun meningkat.

Objektif :

Untuk mengkaji kaitan antara wanita menopos selepas pembedahan dengan hipertensi.

Kaedah Kajian :

Satu kajian retrospective yang dilaksanakan di kalangan wanita selepas pembedahan pembuangan rahim dan kedua-dua ovari atau kedua-dua ovari sahaja yang mendapatkan rawatan di klinik sakit puan di Hospital Univesity Sains Malaysia yang berumur kurang daripada 50 tahun. Faktor-faktor yang dikaji termasuk BMI, bangsa, jumlah kelahiran anak, HRT, sejarah penyakit sendiri seperti kencing manis atau sakit jantung dan sejarah penyakit dalam keluarga.

Kesimpulan:

Purata umur yang dikaji ialah 46.2 tahun. Dalam kajian ini, didapati pesakit yang menjalani pembedahan TAHBSO ialah 97 %, sementara BSO hanya 3 %. Majoriti penyebab pembedahan di kalangan pesakit adalah Fibroid (86.7%) diikuti oleh 'adenomyosis'(5.6%), dan endometriosis (4.3%). Dari kajian ini dapat disimpulkan. bahawa bangsa, berat badan, jumlah kelahiran anak, HRT, sejarah penyakit sendiri seperti kencing manis atau sakit jantung, atau sejarah penyakit dalam keluarga seperti hypertensi, Diabetis Mellitus dan penyakit jantung adalah tidak mempengaruhi berlakunya hypertensi (p>0.050). Akan tetapi, median masa untuk mendapatkan bila akan berlaku hypertensi dalam kajian ini tidak dapat diinterpretasikan kerana kejadian berlakunya hipertensi adalah kurang dari 50%.

ABSTRACT (ENGLISH VERSION)

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF HYPERTENSION AMONG SURGICAL MENOPAUSAL WOMEN AT HOSPITAL UNIVERSITI SAINS MALAYSIA

Introduction:

Surgical menopause defined as attained menopause after surgically removal of uterus with bilateral oopherectomy or removal of both ovaries only. Surgical menopause increases the risk of development of hypertension which is predisposed to the development of the cardiovascular complications.

Objective:

To determined factors associated with the development of hypertension among post-surgical menopausal women.

Method:

A Retrospective study of all surgical menopausal women that was conducted in Hospital University Sains Malaysia. It involved all 301 patients who was surgically menopause and age less than 50 years , attending Gynaecology clinic at HUSM. Race, hormone replacement therapy (HRT), parity, body mass index (BMI), underlying medical illness (diabetes Mellitus(DM)and Cardiovascular Disease (CVS)), smoking status, family history of hypertension, DM and CVS, were recorded retrospectively from medical record .

Result:

The mean age of the patients was 46.2 years old. In this study, we found that most patients had gone through TAHBSO (97.0%) while another three percent (3%) had BSO. The majority of women had a fibroid (86.7%), followed by adenomyosis (5.6%) and endometriosis (4.3%), However, there is no significant association among the factors investigated which include race, age, BMI, parity, HRT, underlying medical illness (DM and CVS), smoking status, family history of hypertension, DM and CVS (p>0.050). Median hypertension survival time could not be reported as hypertensive events occurred less than 50% and the survival probability did not drop to 0.5 (50%) or below. No median survival because most patients survives hypertension.

Conclusion:

The mean age of patient involved in this study was 46.2 years , 97% of patient had undergone TAHBSO and only 3% BSO. There were no significant relationship between hypertension with race, BMI, parity, history of taking HRT, underlying medical illness (DM and CVS), smoking status, family history of hypertension, DM and CVS. There is no median survival rate for hypertension in post-menopausal group as the median hypertension survival time could not be reported as hypertensive events occurred less than 50% and the survival probability did not drop to 0.5 (50%) or below. No median survival because most patients survive hypertension.

1.0 INTRODUCTION

1.1 Menopause

1.1.1 Definition

Menopause is a natural process which is defined as cessation of menses. It is diagnosed retrospectively after 12 consecutive months of amenorrhea for which no other pathological or physiological cause of menopause (World Health Organization, 1981; Kaufert *et al.,* 1986; McKinlay *et al.,* 1985).

Menopause marks the end of reproductive life. Menopause usually occurs naturally in women, or it might be induced surgically after hysterectomy with bilateral oophorectomy or bilateral salpingo-oophorectomy. Surgically induced menopause is termed as surgical menopause. Natural menopause usually undergoes three transition stages; Premenopause, Perimenopause, Postmenopause.

The premenopausal state is defined as menstruation within the prior three months, with no change in the regularity of cycle. Perimenopausal involved the change in cycle regularity or three to eleventh months of amenorrhea. The postmenopausal state consists of permanent amenorrhea which is diagnosed retrospectively.

1.1.2 Changes in Hormone Metabolism Associated With Menopause

Following menopause, there are major changes in androgen, estrogen, progesterone and gonadotrophin secretion following the cessation of ovarian follicular activity (Burger *et al.*, 2002). In postmenopausal women, there is a reduction in circulating androstenedione to approximately 50% of the concentration found in young women. The main estrogen in postmenopausal women is estrone, which mostly derived from peripheral aromatization of androstenedione.

The level of progesterone is also low in post-menopausal women, the level only 30% seen in young women during the follicular phase. Both Luteinising Hormone (LH) and Follicular Stimulating Hormone (FSH) levels rise with FSH markedly higher than LH. The marked increase in circulating gonadotrophin is due to the absence of negative feedback of ovarian steroids hormone and inhibin on gonadotrophin-release hormone (Margerat, 2003). Hypertension is a major predisposing factor for developing cardiovascular disease, especially in a post-menopausal women.

1.1.3 Sequelae of Ovarian Failure

The short-term sequelae of menopause are vasomotor symptoms, mood disorder, urogenital and sexual dysfunction. A study on Malaysian menopause women indicate that only 30% of the complaints of menopausal symptom, of which 57 % of them were having vasomotor symptom such as hot flushes (Nik Nasri,1994). Hot flushes can happen at any time of the day or night. It disturbs sleep if it occur at night. Chronically deprived of sleep will lead to insomnia, irritability, difficulty in concentration and short-term memory loss.

The long-term complication included cardiovascular disease, osteoporosis and tissue atrophy (Brincat et al., 1987).

1.1.4 Hormone Replacement Therapy (HRT)

Hormone replacement therapy contains estrogen only or combined estrogen and progesterone, which can be given continuous or cyclical basis. HRT widely use in the management of climeteric symptoms such as hot flushes, night sweat, vaginal dryness and sleep disturbance . HRT can prevent postmenopausal bone loss and osteoporotic fracture in long-term usage.

1.2 Hypertension

Definition

Hypertension defined as persistent elevation of blood pressure greater than systolic 140 or diastolic Blood pressure more than 90mmHg or taking medication (M Moser-Journal of clinical hypertension, 1999.).

The American Heart Association recommends that need at least three resting measurements on at least two separate health care visits (Journal of the American Society of Hypertension: JASH.5 (4): 259-352.2011). It is a risk factor for developing heart attack and cardiovascular disease. The incidence of cardiovascular disease and atherosclerotic diseases are higher in postmenopausal women (Tunstall-Pedoe H, Lancet 1998).

1.3 JUSTIFICATION TO CONDUCT STUDY

This retrospective study aims to evaluate the risk factors associated with the development of hypertension in post-surgical menopausal women attending gynaecology clinic in Hospital University Sains Malaysia.

Previous studies mainly observe postmenopausal as a general population. There is no specific study regarding post-surgical menopause in relation to the development of hypertension and its associated factor. This study is also important in describing the patterns of hypertension in our community. Also, awareness and knowledge of the study could be instituted and ultimately to improve the diseases , future management and quality of life in post surgical menopausal ladies.

1.4 BENEFITS OF THE STUDY

Retrospectively, the information from this study is crucial to improve future management, plan of action and counselling to the patient in prevention and optimization of hypertensive control in post-surgical menopausal women.

2.0 LITERATURE REVIEW

Globally, life expectancy has improved from the year 2000 to 2015; 68.7 and 73.7 years respectively. Life expectancy for a female is higher compared to male population. World Health Organization has noted that in 2015 female life expectancy was 73.7 years while, male life expectancy was 69.1 years (World Health Organization, 2015).

In Malaysia life expectancy now reaches 77.4 years in women and 72.5 years in male (Department of statistic Malaysia,2015). Despite the improvement of women life expectancy, the average age of menopause remains at 47.96 years (Jahanfar *et al*., 2006). Studies also have shown that the median age of menopause in Malaysia women is 48.7 years (Hamid *et al*., 1989) and 50.7 years (Nik Nasri, 1994).

Women are now living more than one-third of life in menopausal years. Thus, it is important for the clinician to understand the hormonal and physiological changes of menopause and also psychological aspects that are associated with it. It is important in the preventing, identification and management of related medical illness.

Following menopause, there are major changes in androgen, oestrogen, progesterone and gonadotrophin secretion, which occur due to the cessation of ovarian follicular activity (Burger *et al.,* 2002).

In postmenopausal women, there is a reduction in circulating androstenedione to approximately 50% of the concentration found in young women.The main estrogen in postmenopausal women is estrone, which largely derived from peripheral aromatization of androstenedione.

The level of progesterone is also low in post-menopausal women, being only 30% seen in young women during the follicular phase. Both LH and FSH levels rise with FSH markedly higher than LH. The marked increase in circulating gonadotrophin is due to the absence of negative feedback of ovarian steroids hormone and inhibin on gonadotrophin-release hormone (Margerat, 2003).

The short-term sequelae are vasomotor symptoms, mood disorder, urogenital and sexual dysfunction. Study of menopause among Malaysian women only 30% of the complaints of menopausal symptom, 57 % were due to vasomotor symptom such as hot flushes

(Nik Nasri,1994).

Hot flushes can happen any time of the day or night, which will disturb sleep at night. Chronically deprived of sleep will lead to insomnia, irritability, difficulty in concentration and short-term memory.

The long-term complication are cardiovascular disease, osteoporosis and tissue atrophy due to the deficiency of estrogen to support postmenopausal women (Brincat et al., 1987).

Biological changes occurring as a result of menopause are difficult to evaluate since menopause coincides with ageing, and menopause and blood pressure are jointly influenced by factors, such as body mass index, socio-economy class and smoking.

With the use of Cochren-Mantel-Haenszel method, both natural and surgical menopause were associated with 0.5 mmHg /year steeper rise in systolic blood pressure with age. Also, postmenopausal women, had an average of 2.3 mmHg higher diastolic blood pressure then premenopausal (Jan Staessen *et al*.,1989).

Hypertension is estimated to cause 4.5% of the global disease burden and is as prevalent in many developing countries as in developed countries (WHO, International society of hypertension 2003). Worldwide, seven million premature deaths attributed to hypertension (WHO, The World Health Report: Reducing Risk, Promoting Healthy Life 2002).

In recent decades, it has become increasingly clear that the development of stroke, ischemic heart disease, and renal failure have been attributed to hypertension. Treating hypertension has been associated with a 40% reduction in the risk of stroke and about 15% reduction in the risk of myocardial infarction (WHO, International society of hypertension 2003).

There is a positive relationship between systolic blood pressure (SBP), diastolic blood pressure (DBP) and the risk of developing cardiovascular, cerebrovascular and renal diseases. Therefore the main aim of identifying and treating high BP is to reduce these risks. Hence BP should be measured at every clinic encounter (CPG, management of hypertension 3rd edition 2008).

Hypertension is a major risk factor for cardiovascular disease, which is the leading cause of mortality and morbidity in postmenopausal women (Wassertheil-Smoller *et al.*, 2000). After menopause, the sharp increase in the prevalence of hypertension to levels that equal or surpass that of men suggest that premenopausal women state is protection against hypertension (Khalil RA. *et al.*, 2005).

There is evidence that blood pressure may not be as well-controlled in women as in men, despite the fact that most women adhere better to their therapeutic regimens and medications better than men, and have their blood pressures measured more frequently than men. (Hypertension Journal, June 2012,Volume, Issue 3). Postmenopausal women have been shown more salt sensitive than premenopausal women (Myers K *et al.*, 1983).

Postmenopausal was an independent risk factor for hypertension (Ying Zhou *et al*., 2015). Other known risk factors for hypertension included body mass index (BMI), abdominal obesity, family history of cardiovascular disease among the first-degree relatives, a personal history of diabetes, and high triglyceride (Ying Zhou *et al*., 2015). Menopause is also accompanied by weight gain (Portaluppi. F *et al*, Hypertension 1997).

The incidence of cardiovascular disease and atherosclerotic diseases are higher in postmenopausal women (Tunstall-Pedoe H, Lancet 1998) and hypertension is a known risk factor for cardiovascular disease.

Aging and natural menopause were difficult to define. When the exact timing of menopause is still unknown. This is due to the lack of concurrent measurement of hypothalamic and reproductive hormones to distinguish menopause from other cause of amenorrhea and differentiation between late pre-menopause, perimenopausal, and early menopause (Brittner V, 2009).However, in surgical menopause there is an abrupt cut off the supply of ovarian hormone especially endogenous estrogen.

Surgical menopause causes abrupt loss of ovarian hormone, independent of ageing, was associated with the development of salt-sensitive in a substantive number of previously salt resistant women. Women are classified as salt-sensitive was significantly greater four months after surgical menopause (Schulman *et al.*, 2006).

After menopause, the loss of the ovarian hormones predisposes women to salt sensitive and hypertension that would be at higher risk for cardiovascular morbidity and mortality.

The post menopausal estrogen deficiency may affect the balance between various vaso-active hormone and the proliferation and function of vascular smooth muscle cells, possibly by altering the electrolyte composition. Menopause through a redistribution of body sodium and the cessation of periods is followed by a rise in haemoglobin and in erythrocyte count (Hjortland MC. *et al* ,Am J Epidemiol 1976), therefore increasing blood viscocity and in turn possibly also blood pressure(Yarnell JWG *et al*,Circulatioin 1991).

The present observation may have important implication for cardiovascular disease. Salt-sensitive hypertensive patient has a higher incidence of left ventricular hypertrophy, (Heimann JC *et al*., 1991) endothelial dysfunction, (Miyoshi A *et al*., 1997) hyperlipidemia (Bigazzi R.*et al*.,1994), and microalbuminemia (Bigazzi R *et al*.,1994) compare to the salt-resistant hypertensive patient. Also, an association between insulin resistance and salt sensitive in non-diabetic, non- obese, essential hypertensive subjects has been reported (Suzuki M *et al.*, 2000).

Estrogen therapy after menopause demonstrate that correction of postmenapausal estrogen deficiency is accompanied by a decrease in the incidence of cardiovascular complication (JA Staessen *et al,* Journal of Human Hypertension,1998).

3.0 OBJECTIVES OF THE STUDY

3.1 General Objective

- To evaluate hypertension in surgical menopausal patients.

3.2 Specific Objective

- To determine the prevalence of hypertension among patients with surgical menopause at HUSM .

- To determine the timing of onset of hypertension in post TAHBSO and BSO at HUSM.

- To determine the factors associated with the onset of hypertension in post-surgical menopause patients.

4.0 METHODOLOGY

This study was a retrospective which was done in Hospital University Sains Malaysia. The record of all patients who had undergone TAHBSO from 1st January 2000 to 31st December 2010 were reviewed.

4.1 Sample Size Calculation

The estimated sample size for the third objective was calculated based on the study done in northeast China which stated that post menopause status was an independent risk factor for hypertension.(Ying Zhou et.al.2014) using PS software sample size with 2 min formula. $n = Z\alpha$

Variable	A	M	P	σ	Δ (20% less fr SD)	nx3	
Age	0.5	2	0.8	7.8	5	19 x 3	57
BMI	0.5	2	0.8	3.9	3	19 x 3	57
FBS	0.5	2	0.8	1.8	2	20 x 3	60

n= sample size

2 proportion formula

Variable	A	P	M	P0	P1	N	
Smoking	0.05	0.8	2	10	20	143 x 2	286

Based on the above calculation, a minimal of 314 patients were needed to meet the 80% statistical power.

4.2 Inclusion criteria

All post total abdominal hysterectomy with bilateral oophorectomy or bilateral oophorectomy women for the benign disease at the age less than 50 years old and follow up at Gynecology clinic HUSM from January 2000 to December 2010.

4.3 Exclusion criteria

Patients with the following criteria were excluded from the study:

1. Surgery performed for malignant disease.
2. Pre-existing hypertension.
3. Incomplete data.

4.4 Ethical and Consent

An approval to conduct the study was obtained from the Human Research Ethics Committee USM (HREC). The consent to review the medical records was obtained from director of Hospital University Sains Malaysia.).

4.5 Data Collection

The list of patients who had undergone TAHBSO and BSO in Hospital University Sains Malaysia was obtained from the Hospital USM's O&G clinic. The case notes of patients were obtained from the record office. Data was collected and entered in the Clinical Research Form as shown in Appendix : 1

4.6 Data Entry and Analysis

All data were analysed using SPSS version 24. For descriptive analysis, continuous or numerical variables were described in mean and categorical variables were described in frequency and percentage (%). Data was analysed based on specific objectives. Chi-Squared test and differences in mean were used for categorical and continuous variables.

To evaluate the association between measured variables such as the indication for operation, BMI, the age of operation, ethnic group, socioeconomic status, the age of menarche and parity of post-surgical menopausal patient. Multiple logistic regression and survival analysis were performed.

All factors with the p value less than 0.05 (significant level) in the univariate analysis were included in the multivariate analysis.

4.7 FLOW CHART

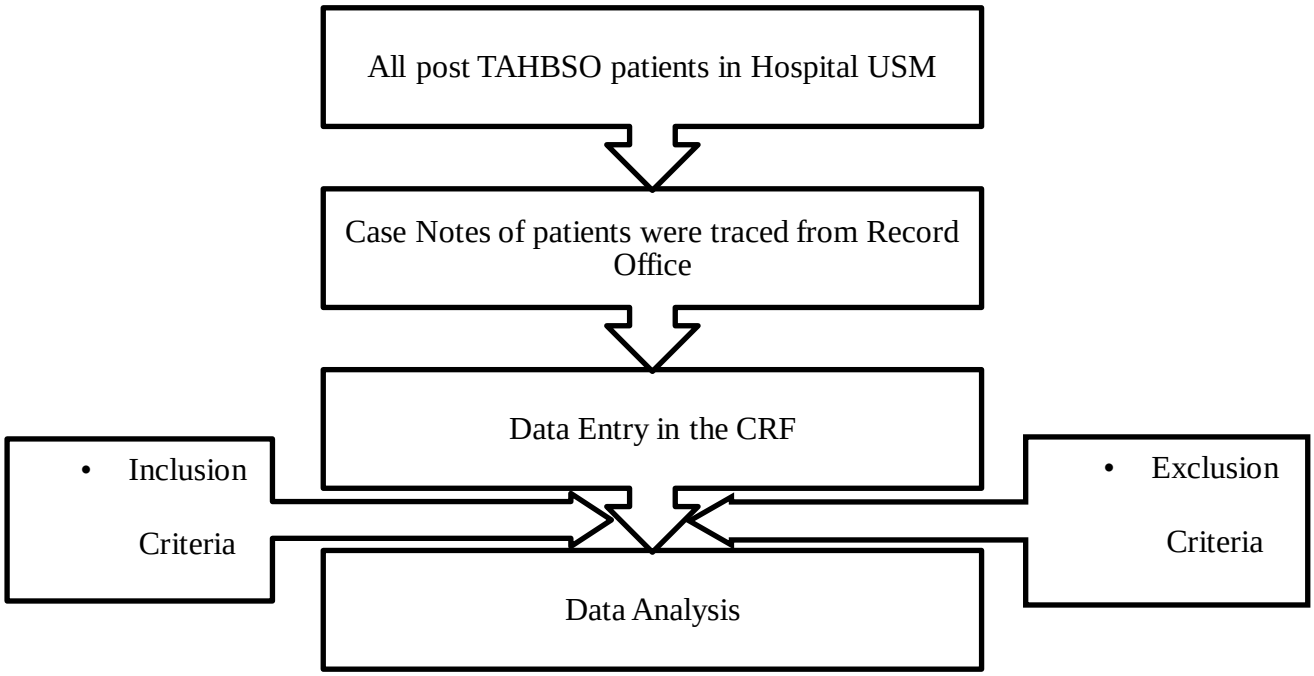

Figure 1: Study flow chart

5.0 RESULTS

5.1 Demographic data

A total of 301 patients were recruited into the study. The age of the patients recruited ranged from 30-50 years old. The mean age of the patients was 46.2 +/-2.99 years (Figure 2).

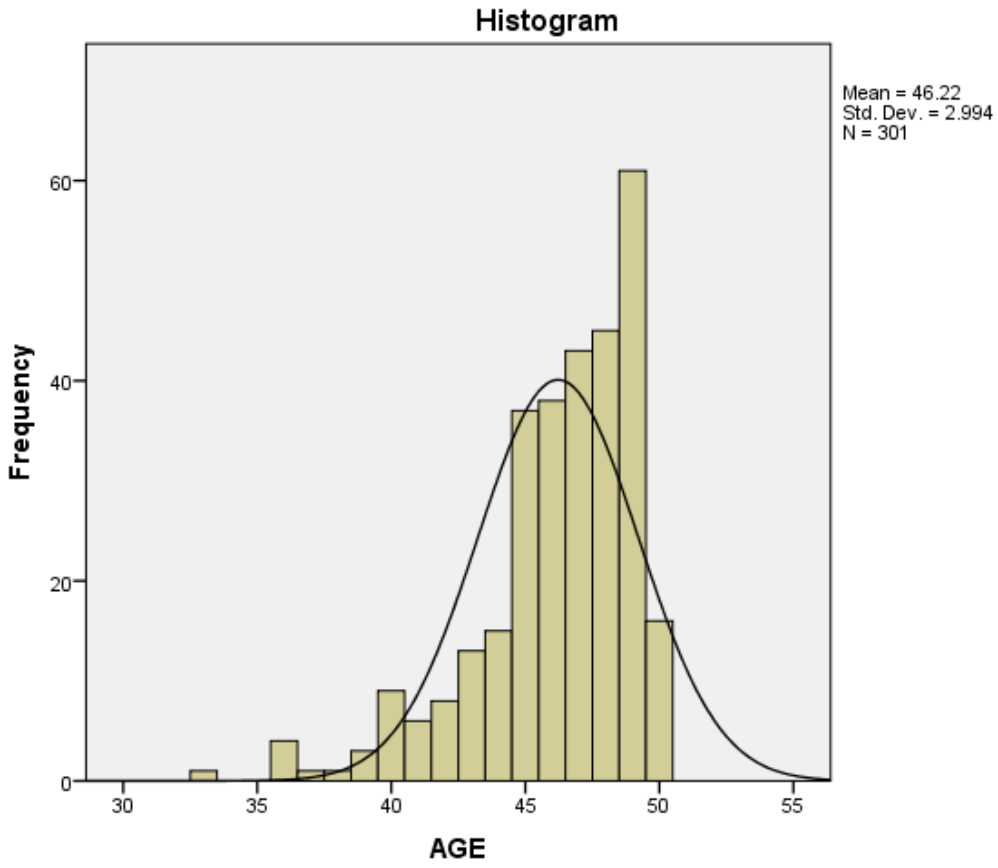

Figure 2: Histogram showing the age distribution of the patients.

Most of the patients had normal BMI ; with mean BMI of 26.0 +/- 6.5 kg/m2. The lowest BMI was 17 kg/m2 and the highest was 41.7 kg/m2.

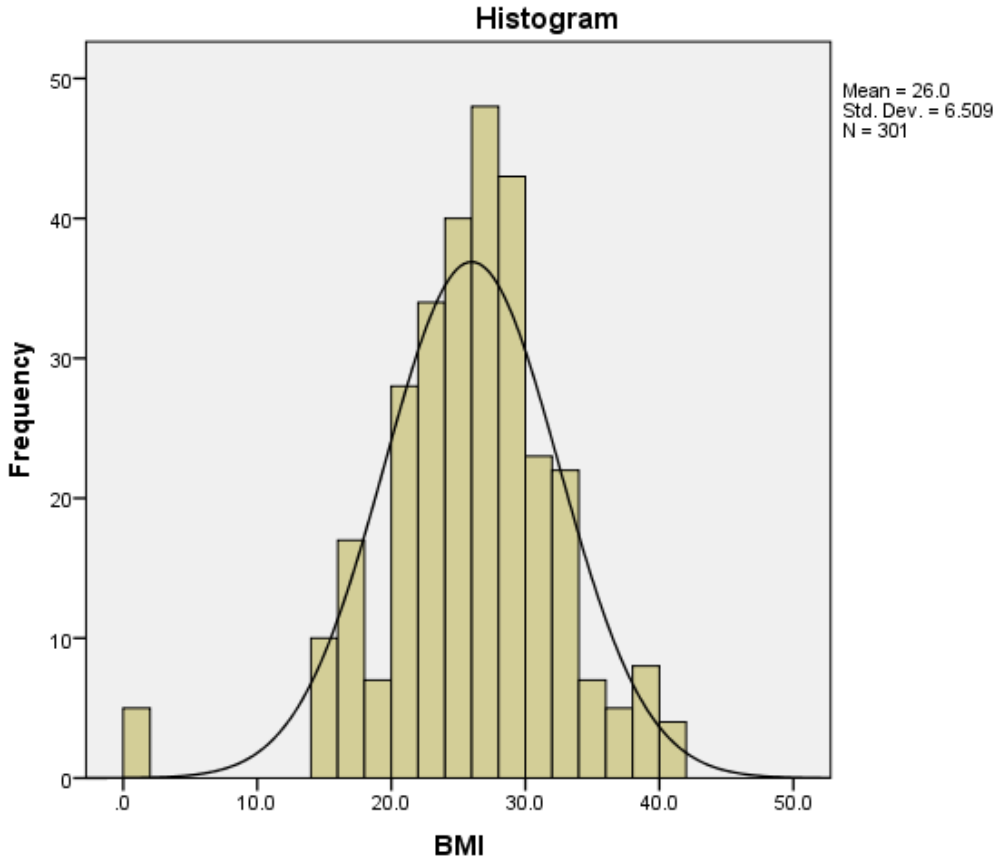

Figure 3 : Histogram showing distribution of BMI

79% of the patients (n=238) were Malay, 18.94% (n=57) were Chinese and the rest (2.0% ,n=6) were Indian and Siamese (Figure 4).

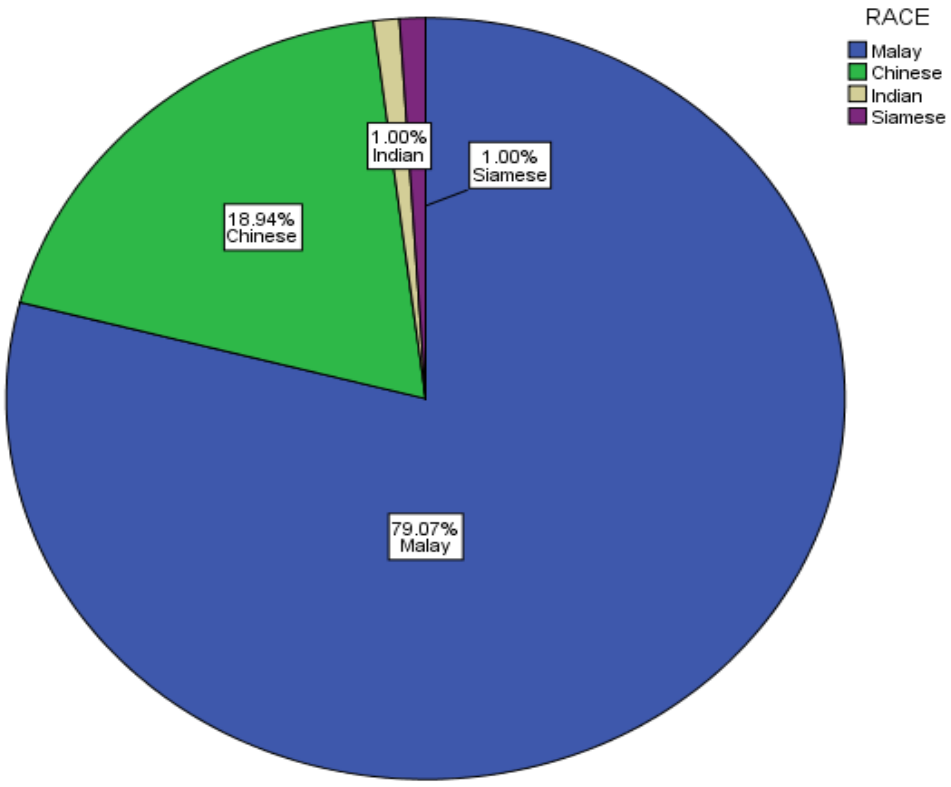

Figure 4 : Ethnicity of post -surgical menopausal patient at HUSM.

More than 90% of the patients had undergone TAHBSO (n=292 ; 97%) and only 9 patients (3.0%) underwent BSO. Table 1 shows the indications for the operations.

Table 1: Types of operation and indication of surgical procedure among post-surgical menopausal women

Variables	Post surgical menopausal women
	n (%)
Types of operation	
TAHBSO	292 (97.00)
BSO	9 (3.00)
Indication	
Fibroid	261 (86.71)
Adenomyosis	17 (5.64)
Endometriosis	13 (4.32)
Bilateral teratoma	7 (2.33)
Bilateral endometriosis	2 (0.66)
Ovarian cyst	1 (0.34)

TAHBSO: Total abdominal hysterectomy bilateral salpingo-oophorectomy

BSO: Bilateral salpingo-oophorectomy

Most of the patient were nulliparous and had low parity , nulliparous 18.3% (n:55) ,followed by parity four 16.9 % (n: 51), parity three ,16.3 % (n:49), parity one ,11.3% (n:34)

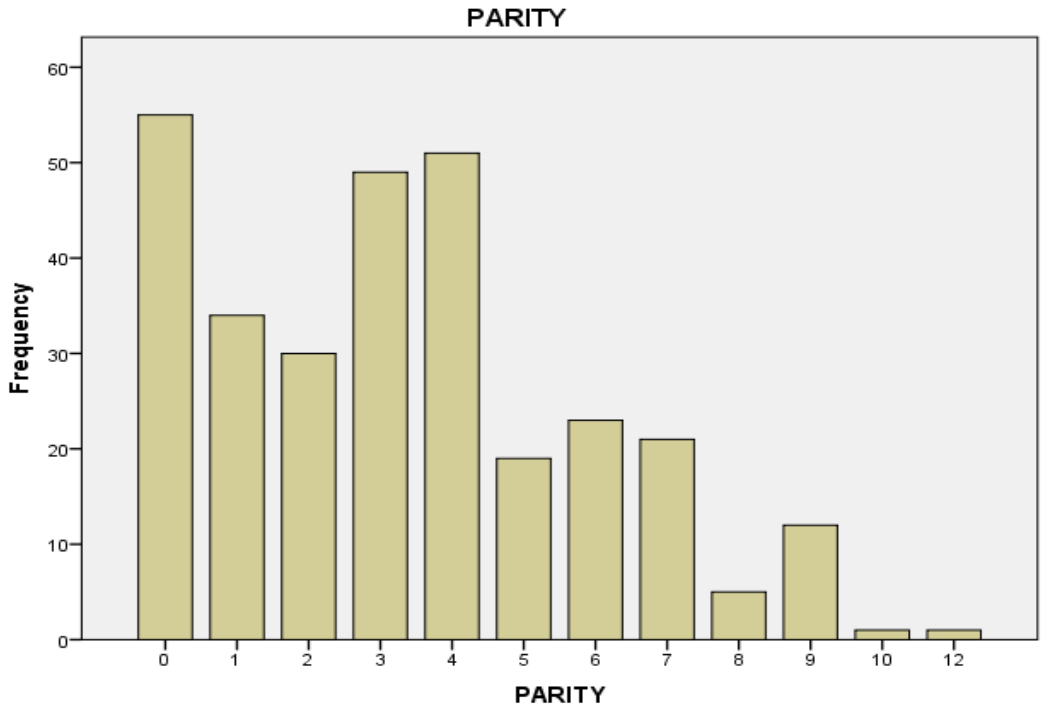

Figure 5: Histogram showing the frequency of the parity of the patients

59.1% of the patients received Hormone Replacement Therapy (HRT) after operation (n:178). Otherwise 40.9% (n: 123) of patient did not received HRT.

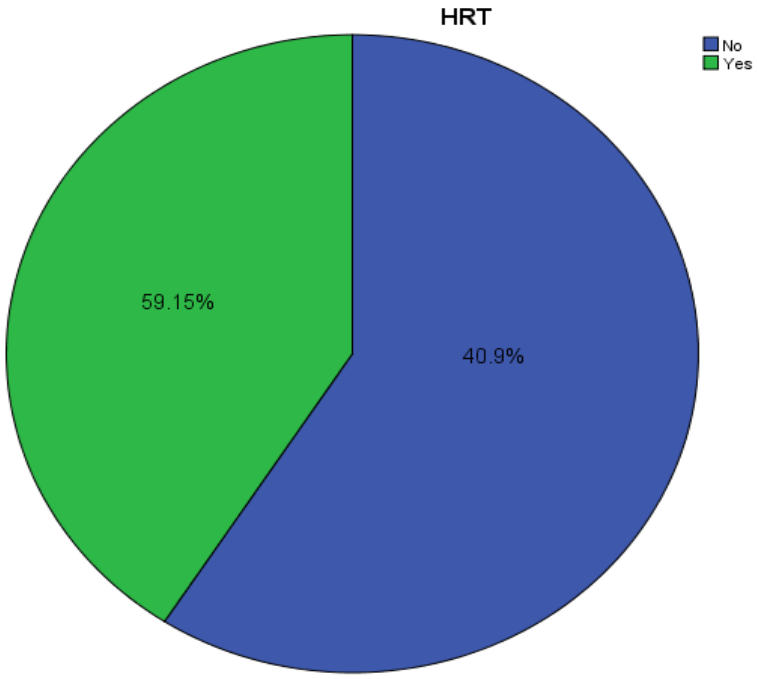

Figure 6: Pie chart showed the percentage of HRT in post operation patients.

5.2 Prevalence of hypertension

Out of the 301 surgical menopause patients, only 82 of them (27.0%) were noted to have hypertension, as was shown in Figure 5

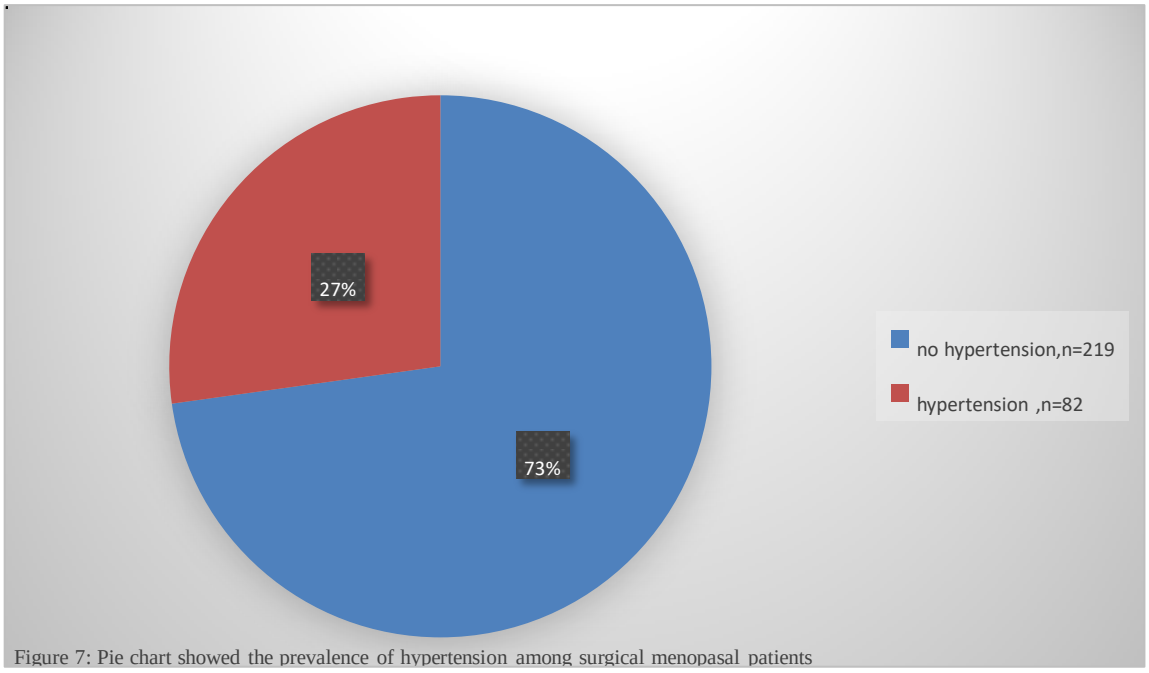

Figure 7: Pie chart showed the prevalence of hypertension among surgical menopasal patients

Figure 7: Pie chart showed the prevalence of hypertension among surgical menopausal patients.

5.3 Comparison of the demographic data and medical background between the hypertensive and non-hypertensive group.

The demographic data and medical background of the patients with and without hypertension was compared (Table 2)

Table 2: Comparison of the demographic data and medical background among patients with and without hypertension.

Variables	Hypertensive (n=82) n (%)	Non hypertensive (n=219) n (%)	*p* value
Sociodemographic			
Race			
Malay	65 (79.30)	173 (79.00)	>0.950 [b]
Chinese	15 (18.30)	42 (19.20)	
Indian	1 (1.20)	2 (0.90)	
Siamese	1 (1.20)	2 (0.90)	
Mean age	46.54(2.37)	46.11(3.19)	0.205
Mean parity	3.70(2.05)	3.16(2.74)	0.069
Mean BMI	27.05(5.33)	25.6(6.87)	0.086
HRT			
Yes	33 (40.20)	90 (41.10)	0.894 [a]
No	49 (59.80)	129 (58.90)	
Medical illness			
DM			

Yes	0 (0.0)	4 (1.8)	0.578 [b]
No	82 (100.0)	215 (98.2)	
CVS			
Yes	0 (0.0)	0 (0.0)	[c]
No	82 (100.0)	219 (100.0)	
Smoker			
Yes	0 (0.0)	0 (0.0)	[c]
No	82 (100.0)	219 (100.0)	
Family History			
Hypertension			
Yes	1 (1.2)	2 (0.9)	>0.950 [b]
No	81 (98.8)	217 (99.1)	
DM			
Yes	1 (1.2)	0 (0.0)	0.272 [b]
No	81 (98.8)	219 (100.0)	
CVS			
Yes	0 (0.0)	0 (0.0)	[c]
No	82 (100.0)	219 (100.0)	

[a] Pearson Chi-Square test

[b] Fisher's exact test

[c] No statistics are computed because the variable is a constant

5.4 Duration of onset of hypertension

As previous stated in section 5.2 , 82 surgical menopausal patients were noted to develop hypertension. The earliest duration of onset of hypertension was 2 months (n :32, 10.6 %) after operation and the longest duration was 5 years (n: 1, 0.3%). The mean duration of onset of hypertension was 5.65 months +/-8.44 months post surgery .

The Kaplan –Meier Hypertension Survival Analysis was used to predict the probability of the onset of hypertension among the surgical menopausal patient. The median hypertension survival time could not be reported as the prevalence of hypertension among this group of patients was less then 50%, and the survival probability did not drop to 0.5 (50%) or below (as showed in Figure 8).

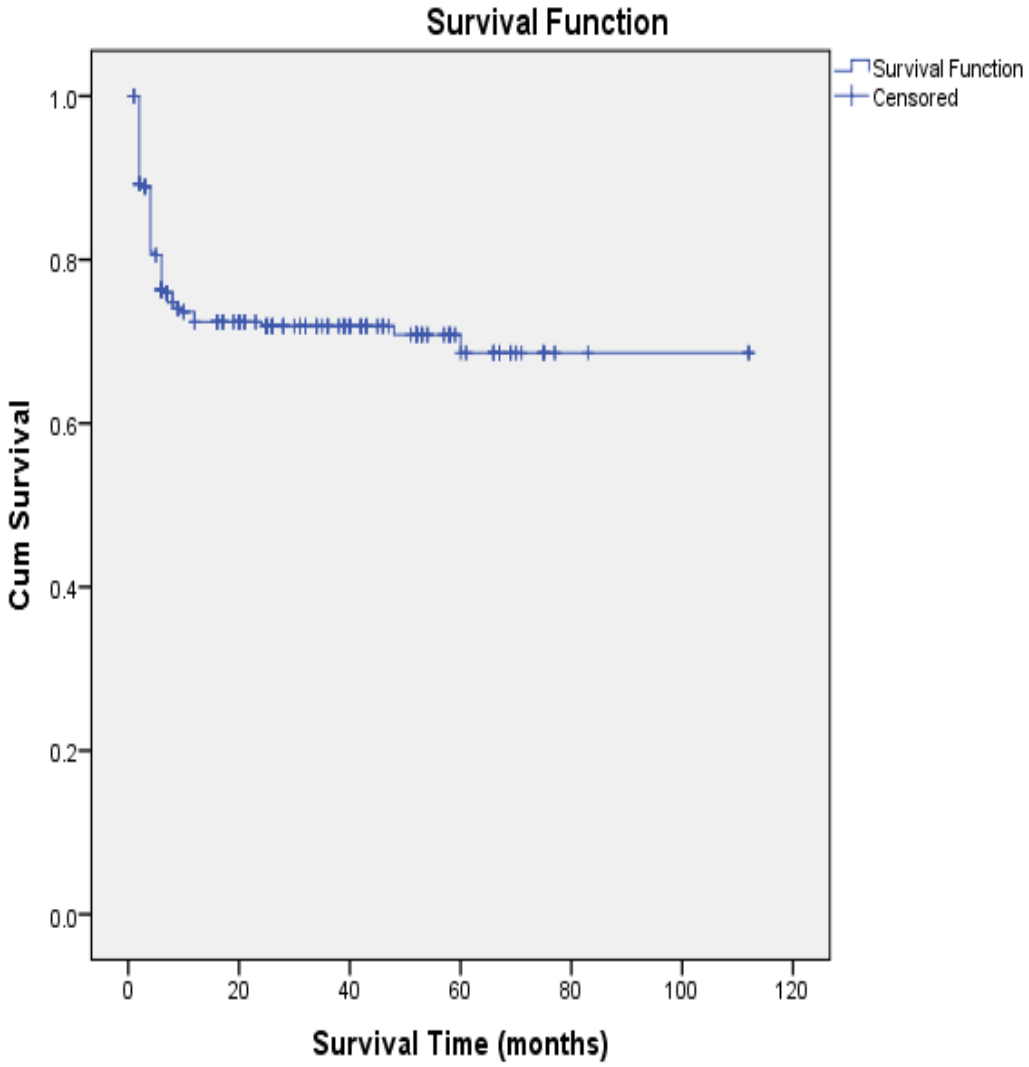

Figure 8: Kaplan-Meier curves of hypertension survival estimate among post-surgical menopausal women in Hospital USM (n=301).

5.5 Factors associated with the development of hypertension

From the univariate analysis as stated in Table 3, it was noted that factor such as age, parity, BMI, family history of hypertension, preexisting medical illness such as Diabetes Mellitus, smoking and hormone replacement therapy were not significantly associated with the development of hypertension in post surgical menopausal patient.

6.0 DISCUSSION

Postmenopausal status was an independent risk factor for hypertension. (Ying Zhou *et al*., 2015). It can be natural menopause or surgically menopause women, the implication of that for both group of women can be the same, they can presented with climacterics symptoms ,psychological genitourinary symptoms, skeletal complains and cardiovascular complication.

In this study, more evaluation and related demographic factors with background of medical illness, specifically hypertension and Diabetes Mellitus were studied. Hypertension is a major factor risk factor for developing cardiovascular disease such as Ischemic heart disease which can cause sudden death. Cardiovascular disease is currently leading cause of mortality among postmenopausal women.

In this study, surgical menopausal women were selected retrospectively who attend Gynaecology clinic University Sains Malaysia Hospital to determine factors associated with the development of hypertension among post-surgical menopause women between January 2000 to December 2010 at Kubang Kerian, Kelantan.

Overview of surgical menopausal women at Hospital University Sains Malaysia, Most of the patients in University Sains Malaysia Hospital went through TAHBSO (97.0%, n: 292) while another three percent had BSO (n: 9).

The majority of women went through operation had uterine fibroid (86.7%), followed by adenomyosis (5.6%) and endometriosis (4.3%).This is consistent with most literature review uterine fibroid is the most common gynaecology tumour (prevalence 20-25%).

In term of age, mean age of the patient in the study population was 46.2 years. This is consistent with most studies, as TAHBSO or BSO is considered for women after the age of 45 years old. We opted for conservative and medical management of this gynaecology disorder before embarked on surgical option which would render the patient surgically menopause.

Most patient underwent TAHBSO, 97% (n: 292), only 9 patient (3.0%) underwent BSO. The minority group , mostly operation due to Endometriosis, they have to underwent multiple operation for symptomatic causes and finally both ovaries were removed at premenopausal age.

Otherwise, in term of BMI, mean BMI of the patient was 26.0 +/- 6.5 kg/m2, which included in overweight group. This finding consistent with in another study at northeast China found that overweight and obesity were associated with a 1.97-fold and 2.97-fold increased for hypertension respectively (Ying Zhou at. al., Maturitas 80 (282–287.) 2015).

Regarding ethnicity, majority patient are of Malay ethnicity 79% (n: 238). Followed by Chinese 18.94% (n=57) . This is due to the study population were observed in Kelantan, where the majority were Malay.

Most of the patient were nulliparous and had low parity , nulliparous 18.3% (n:55) , followed by parity four 16.9 % (n: 51), parity three ,16.3 % (n:49), parity one 11.3% (n: 34) . These findings are comparable to most reported studies, as uterine fibroid and endometriosis are significantly associated with nulliparous and low parity.

Patient who received Hormon Replacement Therapy 59.1% (n : 178). Otherwise 40.9% (n: 123) of patient did not received HRT. Most patient were given HRT due to the climacteric symptoms after excluded the risk of breast carcinoma in selected HRT group. Another 40.9 % group who did not received HRT, refused HRT and family history of breast carcinoma after full counseling given. In postmenopausal women, treatment of arterial hypertension and glucose intolerance should be priorities. Observational studies and randomized clinical trials suggest that hormone replacement therapy (HRT) started soon after the menopause may have cardiovascular benefit.

Most of patient did not had preexisting Diabetes Mellitus , family history of hypertension and cardiovascular disease and non-smoking, as majority were without any comorbid prior to operation .). Furthermore, all women do not have CVS and were the non-smoker. Thus, no statistics were computed because the variables were constant.

Out of the 301 patient, only 82 of them (27.0%) were having hypertension and 219 (73.0%) patient were free of hypertension. Comparison between demographic data and medical background between hypertension and non hypertension group noted that there were no significant correlation between mean age, mean parity , mean BMI ,race, smoking status, medical illness such as Diabetes Mellitus, HRT, and family history of Hypertension, Diabetes Mellitus and cardiovascular disease with the development of hypertension .

This study result was dissimilar with study done by Ying Zhou 2015 at china , which stated that other known risk factors for hypertension included body mass index (BMI), abdominal obesity, family history of cardiovascular disease among the first-degree relatives, a personal history of diabetes, and high triglyceride. Time frame of the study may need to extend up to 20 years in future ,to follow up and evaluate patient outcome.

For patient who developed hypertension, only 33 patients were on HRT (40.20%) and 49 patients were not on HRT (59.80%). However, in non hypertensive patients , 90 patients with HRT(41.0%) and 129 patients not on HRT(58.9%), This statistical study showed that no significant relation between development of hypertension and patients on HRT. Patients on HRT or not did not influenced the development of hypertension in surgical menopausal women .

There were no significant relationship between family history of medical disease such as hypertension, Diabetes Mellitus, cardiovascular disease, medical illness such as hypertension and Diabetes Mellitus, and smoking with development of hypertension. This is due to most of the patients were premorbid healthy without any medical illness.

The overall cumulative hypertension survival probability curve for 301 post-surgical menopause women from 2001-2010 was shown by Kaplan-Meier curve in Figure 8. The Kaplan –Meier Hypertension Survival Analysis was used to predict the probability of the onset of hypertension among the surgical menopausal patient. The median hypertension survival time could not be reported as the prevalence of hypertension among this group of patients was less then 50%, and the survival probability did not drop to 0.5 (50%) or below. May need larger sample size and longer duration of the study to positively predict the development of hypertension.

There are five associated factors which were studied to find the association with the development of hypertension among surgical menopausal women. Among 301 surgical menopausal women involved in this study, only 82 women (27.2%) developed hypertension while 219 women (72.8%) were non-hypertensive. The majority of the women were Malay (79.1%) and Chinese (18.9%), while Indian and Siamese were only 1.0% respectively. Among the hypertensive women, 79.3% were Malay, and 18.3% were Chinese. However, there was no significant association between race and hypertension development (p>0.950).

7.0 CONCLUSION

Overall 301 post-surgical menopausal women were included in this study. The mean age of the women was 46.2 years old. In this study, we found that most patients had gone through TAHBSO (97.0%) while another three percent (3%) had BSO. The majority of women had a fibroid (86.7%), followed by adenomyosis (5.6%), endometriosis (4.3%). The study showed ,there are no significant relationship between hypertension in post-surgical menopause in BMI, parity, ethnic group, HRT, underlying medical illness (DM and CVS), smoking status, family history of hypertension, DM and CVS using Pearson Chi-square test and Fisher exact test. The overall cumulative hypertension survival probability curve for 301 post-surgical menopause women from 2000-2010 was shown by Kaplan-Meier curve, the median hypertension survival time could not be reported as hypertensive events occurred less than 50% and the survival probability did not drop to 0.5 (50%) or below, which mean no median survival because most patients survived without hypertension in post-surgical menopause women . The overall cumulative survival probability for women who had TAHBSO higher than cumulative survival probability for women who had undergone BSO.

8.0 LIMITATION OF STUDY

It is a retrospective study; all data is extracted from HUSM medical record department. The data is from year January 2000 to December 2010 in gynaecology Clinic at HUSM. The incomplete or missing record was discarded. Same of the patient, after hysterectomy and bilateral oophorectomy or bilateral oophorectomy, follow up else way and no record or latest update available at HUSM. The sample population in this study was limited to postmenopausal women who attended gynaecology clinic only, and it does not include representative the whole population of Malaysia

9.0 RECOMMENDATION

This is an interesting and important subject to study, which needs larger sample size and includes multiracial involvement and involving others selected state in Malaysia with a comparable number.

Post-surgical menopause women should receive education and counselling on lifestyle modification to reduce the risk of hypertension and subsequently reduce risks of uncontrolled hypertension complication such as cardiovascular disease, stroke, and renal disease. Evidence-based prevention for the diseases noted above include lifestyle management, cessation of smoking, curtailing excessive alcohol consumption, a healthy diet and moderate exercise, as well as mentally stimulating activities. Beside that , healthy women aged 50–59 years, estrogen therapy can decreases coronary heart disease and all-cause mortality; this interpretation is entirely consistent with results from other randomized, controlled trials and observational studies. Thus. as part of a comprehensive strategy to prevent chronic disease after menopause, menopausal hormone therapy, particularly estrogen therapy may be considered as part it.

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11.0 APPENDICES

Appendix 1: Clinical Research Form (CRF)

Department of Obstetrics and Gynaecology

Faculty Health Science

Hospital University Science Malaysia

Kelantan

DATA COLLECTION SHEET

DEMOGRAPHY PROFILE

1. Identification data

Age :

Race :

2. Biometric measurements

Weight on admission :

Height on admission :

BMI :

Blood pressure on admission:

Blood pressure on the first visit to clinic : BP :

Duration :

Blood pressure on the latest visit: BP :

Duration :

3. Socio-economic profile

Status : single/married/divorced

Job : yes, state the occupation_____

: no

4. Reproductive profile

Menarche :

Parity:

First child :

Last child :

5. Menopausal profile

Operation date :

Operation performed :

Indication :

HPE report :

HRT: yes/no

6. Medically related illness profile

HPT: yes/no

DM: yes /no

Heart disease: yes/no

Smoker: yes/no

7. Family profile

HPT: yes/no

DM: yes/no

Heart disease: yes /no

Appendix 2: Ethical approval

Jawatankuasa Etika Penyelidikan Manusia USM (JEPeM)
Human Research Ethics Committee USM (HREC)

Universiti Sains Malaysia
Kampus Kesihatan,
16150 Kubang Kerian,
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19th April 2017

CR-6533-952

Dr. Ahaddiah Dahian
Department of Obstetrics & Gynecology
School of Medical Sciences
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

JEPeM Code : USM/JEPeM/16120587
Protocol Title : Factors Associated with Development of Hypertension among Post-Surgical Menopause Women at Hospital USM between January 2000 to December 2010.

Dear Dr.,

We wish to inform you that your study protocol has been reviewed and is hereby granted approval for implementation by the Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM). Your study has been assigned study protocol code **USM/JEPeM/16120587**, which should be used for all communication to the JEPeM-USM related to this study. This ethical clearance is valid from **19th April 2017** until **18th April 2018.**

Study Site: Hospital Universiti Sains Malaysia.

The following researchers also involve in this study:
1. Assoc. Prof. Dr. Shah Reza Johan Noor

The following documents have been approved for use in the study.
1. Research Proposal

In addition to the abovementioned documents, the following technical document was included in the review on which this approval was based:
1. Data Collection Sheet

Attached document is the list of members of JEPeM-USM present during the full board meeting reviewing your protocol.

While the study is in progress, we request you to submit to us the following documents:
1. Application for renewal of ethical approval 60 days before the expiration date of this approval through submission of **JEPeM-USM FORM 3(B) 2015: Continuing Review Application Form.** Subsequently this need to be done yearly as long as the research goes on.
2. Any changes in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, must be submitted or reported using **JEPeM-USM FORM 3(A) 2015: Study Protocol Amendment Submission Form.**
3. Revisions in the informed consent form using the **JEPeM-USM FORM 3(A) 2015: Study Protocol Amendment Submission Form.**
4. Reports of adverse events including from other study sites (national, international) using the **JEPeM-USM FORM 3(G) 2014: Adverse Events Report.**
5. Notice of early termination of the study and reasons for such using **JEPeM-USM FORM 3(E) 2015.**
6. Any event which may have ethical significance.
7. Any information which is needed by the JEPeM-USM to do ongoing review.

8. Notice of time of completion of the study using **JEPeM-USM FORM 3(C) 2014: Final Report Form.**

Please note that forms may be downloaded from the JEPeM-USM website: **www.jepem.kk.usm.my**

Jawatankuasa Etika Penyelidikan (Manusia), JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

Thank you.

"ENSURING A SUSTAINABLE TOMORROW"

Very truly yours,

PROF. DR. HANS AMIN VAN ROSTENBERGHE
Chairperson
Jawatankuasa Etika Penyelidikan (Manusia) JEPeM
Universiti Sains Malaysia

Jawatankuasa Etika Penyelidikan Manusia USM (JEPeM)
Human Research Ethics Committee USM (HREC)

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Date of meeting : 2nd March 2017
Venue : Meeting Room, Division of Research & Innovation, USM Kampus Kesihatan.
Time : 9.00 a.m – 2.30 p.m
Meeting No : 355

Members of Committee of the Jawatankuasa Etika Penyelidikan (Manusia), JEPeM Universiti Sains Malaysia who reviewed the protocol/documents are as follows:

Member (Title and Name)		Occupation (Designation)	Male/ Female (M/F)	Tick (✓) if present when above items, were reviewed
Chairperson : Professor Dr. Hans Amin Van Rostenberghe		Chairperson of Jawatankuasa Etika Penyelidikan (Manusia), JEPeM USM	M	✓ (Chairperson)
Secretary: Mr. Mohd Bazlan Hafidz Mukrim		Science Officer	M	✓
Members :				
1.	Assoc. Prof. Dr. Azlan Husin	Lecturer, School of Medical Sciences	M	✓
2.	Assoc. Prof. Dr. Haslina Taib	Lecturer, School of Dental Sciences	F	✓
3.	Assoc. Prof. Dr. Mohtar Ibrahim	Lecturer, School of Medical Sciences	M	✓
4.	Prof. Dr. Narazah Mohd Yusoff	Lecturer, Advanced Medical and Dental Institute (AMDI)	F	✓
5.	Prof. Dr. Nik Hazlina Nik Hussain	Lecturer, School of Medical Sciences	F	✓
6.	Mrs. Norleha Mohd Noor	Executive Secretary, School of Dental Sciences	F	✓
7.	Associate Professor Oleksandr Krasilshchikov	Lecturer, School of Health Sciences	M	✓
8.	Dr. Soon Lean Keng	Lecturer, School of Health Sciences	F	✓
9.	Mrs. Zawiah Abu Bakar	Community Representative	F	✓
10.	Prof. Dr. Zeehaida Mohamed	Lecturer, School of Medical Sciences	F	✓

Jawatankuasa Etika Penyelidikan (Manusia), JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

PROFESSOR DR, HANS AMIN VAN ROSTENBERGHE
Chairperson
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