RISK FACTOR OF YOUNG BREAST CANCER:

A MULTICENTER STUDY

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DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT

FOR THE DEGREE OF MASTER OF MEDICINE (SURGERY)

SCHOOL OF MEDICAL SCIENCES

UNIVERSITI SAINS MALAYSIA

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ABBREVIATIONS

HPP	- Hospital Pulau Pinang
HSJ	- Hospital Seberang Jaya
OCP	- Oral contraceptive pills
BIRADS	- Breast imaging-reporting data system
HPE	- Histopathological Examination
IDC	- Invasive Ductal Carcinoma
ILC	- Invasive Lobular Carcinoma
DCIS	- Ductal Carcinoma In-Situ

ABSTRAK

Pengenalan

Kanser payudara pada usia muda ditakrifkan sebagai kanser payudara yang menyerang pesakit sebelum usia 40 tahun. Kanser ini berbeza dengan kanser payudara pada pesakit yang lebih berusia daripada segi faktor risiko, sifat biologi dan prognosis. Kajian ini bertujuan untuk mengkaji faktor berlakunya kanser payudara dalam kalangan pesakit kanser payudara pada usia muda di Malaysia untuk tempoh 7 tahun.

Metodologi

Kajian ini adalah kajian kawalan kes retrospektif yang melibatkan pesakit kanser payudara pada usia muda yang menerima rawatan dari Januari 2015 hingga Disember 2021 di Hosital Universiti Sains Malaysia, Hospital Pulau Pinang, Hospital Seberang Jaya dan Institut Perubatan & Pergigian Termaju. Kajian ini direka mengikut kadar 1 kes : 1 kawalan. Pesakit yang memenuhi kriteria kemasukan dan pengecualian diambil masuk ke dalam kedua-dua kategori iaitu kategori kes dan kawalan. Data berkenaan demografi, faktor risiko dan data klinikal-patologi telah dikumpul bersama. Ujian regresi logistik mudah dan berganda telah dijalankan. Pemboleh ubah dengan nilai p kurang daripada 0.05 dianggap sebagai signifikan.

Keputusan

Seramai 268 orang pesakit telah diambil ke dalam kajian ini. Setiap kategori mempunyai 134 orang pesakit. Majoriti pesakit kanser payudara pada usia muda adalah berbangsa Melayu iaitu 86.6% (n =116) diikuti oleh bangsa Cina 9% (n=12), bangsa India 2% (n=3) dan lain-lain 2% (n =3). Purata umur ketika diagnosis adalah 34.3 tahun. Gejala utama yang menyebabkan pesakit tampil adalah ketulan payudara 88.8% (n=119) diikuti oleh kesakitan pada payudara 7.5% (n=10), lelehan dari puting payudara 6.7% (n=9), puting tenggelam 3% (n=4) dan radang payudara 0.7% (n=1). Majoriti pesakit mendapat rawatan semasa kanser payudara telah berada

di peringkat akhir iaitu sebanyak 47.8% (n=64) adalah kanser peringkat 4 manakala 17.2%(n=23) adalah kanser peringkat 3. Dari segi rawatan, 106 (79.1%) pesakit menjalani rawatan kemoterapi sama ada sebagai adjuvan, neoadjuvan atau paliatif. Seramai 116 (86.5%) orang pesakit menjalani pembedahan manakala seramai 18 (13.5%) orang pesakit tidak menjalani sebarang pembedahan. Kebanyakan pesakit menjalani pembedahan mastektomi dan pembuangan kelenjar limfa aksilla (57.9%). Bagi faktor risiko kanser payudara pada usia muda pula, regresi logistik berganda menyimpulkan bahawa terdapat 3 pemboleh ubah yang mempunyai perkaitan signifikan dengan kanser payudara pada usia muda. Pemboleh ubah tersebut adalah umur semasa diagnosis (aOR 1.07, nilai-p 0.0034), waktu simptom bermula (aOR 1.25,1.08,1.48, nilai-p 0.01,0.038,0.017) dan sejarah mengambil pil perancang(aOR 1.9, nilai-p 0.041).

Kesimpulan

Pesakit kanser payudara pada usia muda kebanyakannya datang menerima rawatan pada peringkat akhir (peringkat 3 & peringkat 4). Faktor risiko kanser payudara selepas tamat haid tidak boleh diambil kira untuk pesakit muda kerana hanya sebahagian sahaja faktor risiko yang telah dikenal pasti selama ini pada golongan pesakit tamat haid dapat dibuktikan dalam kajian kami.

Kata kunci

Kanser payudara pada usia muda, faktor risiko, pil perancang

Abstract

Introduction

Young breast cancer is defined as breast cancer that developed before 40 years old. It differs to its older counterpart in terms of risk factors, biological characteristics, and prognosis. This study aims to investigate the risk factors of developing breast cancer among young breast cancer patients in Malaysia for a period of 7 years.

Method

This is a retrospective case-control study involving young breast cancer patients who had treatment from January 2015 till December 2021 in Kelantan and Pulau Pinang, Malaysia. It is designed as a 1 case:1 control ratio study. Patients who fulfill the inclusion and exclusion for both case and control were recruited. The demographics, risk factors and clinic-pathological data were collected and compiled. Simple and multiple logistic regression were performed. Variables with p-value less than 0.05 are considered as significant.

Result

A total of 268 patients were recruited into this study. Each arm has 134 patients. Most of our young breast cancer patient are Malay 86.6% (n =116) followed by Chinese 9% (n=12), Indian 2% (n=3) and others 2% (n =3). Mean age of diagnosis is 34.3 years old. Main symptom at presentation is breast lump 88.8% (n=119) followed by mastalgia 7.5% (n=10), nipple discharge 6.7% (n=9), nipple retraction 3% (n=4) and mastitis 0.7% (n=1). Most of our patients have late stage disease as 17.2% (n=23) were in stage 3 and 47.8% (n=64) in stage 4. In terms of treatment, 106 (79.1%) patients had chemotherapy either as adjuvant, neoadjuvant or with

palliative intent. 116 (86.5%) had surgery while 18 (13.5%) did not have any surgical intervention. Most patients underwent mastectomy and axillary clearance (57.9%). For the risk factors of young breast cancer, multiple logistic regression concluded that there are only 3 variables with significant association with young breast cancer. The variables are age at diagnosis (aOR 1.07, p-value 0.0034, duration of noticing symptom (aOR 1.25,1.08,1.48, p-value 0.01,0.038,0.017) and history of taking oral contraceptive pills (aOR 1.9, p-value 0.041).

Conclusion

Young breast cancer mostly present as a late stage (stage 3 & stage 4) disease. The risk factors of post-menopausal breast cancer cannot be applied to this group of patient as only few of the established risk factors were significant in our study.

Keywords

Young breast cancer, risk factor, oral contraceptive pill

Chapter 1

Introduction

Breast cancer is the most common cancer among women within 161 countries and the most common cause of cancer death in 98 countries (1). As for Malaysia, according to the latest cancer registry, it is the most common cancer affecting Malaysian women (2). It is also mentioned that based on current evidence, the incidence of breast cancer increases after 25 years old (2).

Young breast cancer is defined as breast cancer that developed before 40 years old (3) It is considered uncommon in western countries as latest study suggest that it only constitutes 4% of new estimated cases in the USA in 2017. Despite that, they still observe that 1 in 68 women will develop the disease by 40 years of age and 1 in 220 before the age of 30.[4] In the contrary, in African countries, it can be up to 1/3 of all breast cancer cases. As for Asian countries, is it estimated to be around 12% - 30 % of the total number of cases (5).

Risk factor of breast cancer can be divided in modifiable and non-modifiable(6). Among the well-established modifiable risk factor are age, gender, family history of breast cancer, age of menarche and breast density. As for modifiable risk factors, they include parity, breast feeding, oral contraceptive pills consumptions, and lifestyle which includes smoking, alcohol intake and obesity. Most of the risk factor were based on postmenopausal cancer patient and for young breast cancer, the effect might be slightly different (7).

Clinically young breast cancer more likely to present with huge tumour and positive nodal involvement (8). Apart from that young breast cancer also differ in term of biological characteristic. They are characterized by higher proportion of grade 3, triple-negative, human

epidermal growth factor receptor 2 (HER2) overexpression, lympho-vascular invasion and lymphocytic infiltration (9). Apart from that, young breast cancer patient also mostly presented as locally advanced or metastatic disease (10).

Management of young breast cancer do not differ much from postmenopausal cancer patient. Diagnosis should come through triple assessment. According to latest Malaysia CPG, for patient less than 35 years old, ultrasound breast is the mode of imaging (2). Treatment will include surgery and systemic therapy and it should be individualised. Negative effects of treatment on young patient includes premature ovarian failure, sexual dysfunction, depression among others(11). Multidisciplinary approach is therefore paramount in treating these patients.

As for prognosis, young breast cancer patient fared worse compare to older age group. In a recent analysis based on the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2008, patients aged <30 and 30–39 years had significantly inferior overall and breast cancer-specific survival than patients aged 40–49 and 50–59 years (12).

Study and research related to this group of patients is scarce and mostly done in western countries. In this study, the aim is to provide data of young breast cancer among local population. Hopefully more research will be done in the future with regards this unique entity as the approach for them is different from the older counterpart in term of risk factors, managements and other challenges that comes with it.

Problem Statement & Study rationale

Risk factors of breast cancer has been well established, but not quite the case with young breast cancer. Most of the research were done in western countries and limited data were available especially among local patients.

This is the first research in Malaysia focusing on investigating the risk factors of young breast cancer. We would like to ascertain the risk factors young breast cancer in local population and analyses its clinicopathological features. With these data, we are hoping that our understanding of the disease improved, and a holistic approach can be developed with regards of this group of patients.

Chapter 2: Study Protocol

Document submitted for Ethical Approval

Protocol JEPeM Code: USM/JEPeM/ 21120841

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Introduction

Breast cancer is the most common cancer among women within 161 countries and the most common cause of cancer death in 98 countries[1]. As for Malaysia, according to the latest cancer registry, it is the most common cancer affecting Malaysian women.[2]

Young breast cancer is defined as breast cancer that developed before 40 years old.[3] It is considered uncommon in western countries as latest study suggest that it only constitutes 4% of new estimated cases in the USA in 2017. Despite that, they still observe that 1 in 68 women will develop the disease by 40 years of age and 1 in 220 before the age of 30.[4] In the contrary, in African countries, it can be up to 1/3 of all breast cancer cases. As for Asian countries, is it estimated to be around 12% - 18 % of the total number of cases.[5]

In term of risk factor, there are slight differences between young breast cancer and its older counterpart. Race, parity, and large body size are factors that may have opposite effects on breast cancer risk in younger and older women. Other factors that should be taken into consideration include a late age at first birth, never having lactated, oral contraceptive use at early ages or of long duration, a family history of breast cancer, and a history of proliferative benign breast disease.[6]

Apart from that young breast cancer also differ in term of biological characteristic. They are characterized by higher proportion of grade 3, triple-negative and human epidermal growth factor receptor 2 (HER2) overexpression, lympho-vascular invasion, lymphocytic infiltration.[7]

As for prognosis, young breast cancer patient fared worse compare to older age group. In a recent analysis based on the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2008, patients aged <30 and 30–39 years had significantly inferior overall and breast cancer-specific survival than patients aged 40–49 and 50–59 years.[8]

Unfortunately, study and research related to this group of patients is scarce and mostly done in western countries. In this study, the aim is to provide data of young breast cancer among local Pulau Pinang patients. Hopefully more research will be done in the future with regards this unique entity as the approach for them is different from the older counterpart in term of risk factors, managements and other challenges that comes with it.

Problem statement and study rationale

Risk factors of breast cancer has been well established, but not quite the case with young breast cancer. Most of the research were done in western countries and limited data were available especially among local patients.

This is the first research in Malaysia focusing on investigating the risk factors of young breast cancer. We would like to ascertain the risk factors young breast cancer in local population and analyses its clinicopathological features. With these data, we are hoping that our understanding of the disease improved, and a holistic approach can be developed with regards of this group of patients.

Literature review

The incidence of young breast cancer differs greatly between continents. In most developed countries, it is estimated that 6 % of all breast cancer were diagnosed before 40 years old[3]. In the contrary, in African countries, it can be up to 1/3 of all breast cancer cases[4]. As for Asian continent, is it estimated to be around 12% - 18 % of the total number of cases[5]

There are many well established risk factors for breast cancer. Those risk factor can be divided into non-modifiable and modifiable risk factors[15]

One of the non-modifiable risk factors is family history of breast cancer. A positive family history of breast cancer increases the relative risk by 3.22[9]. For breast cancer to develop in younger age group of patients, it is more likely to be associated with increased familial risk, especially those harboring gene mutations for example BRCA1, BRCA2 and TP53[10]. Study by Laloo et al, showed that gene mutations were found in about half who had strong family history and in less than 10 % of women with non-familial breast cancer [11].

Early menarche has also been mooted as a risk factor for breast cancer. It has been shown to increase the risk by 1.39 times for luminal breast cancer[12]. Each one-year delay of menarche has been shown to decreases the risk of breast cancer by 5%[13]. Moreover, the collaborative group on hormonal factors reported up to an 18% reduction in risk in those girls experiencing a late menarche (≥ 13), compared to those who began cycling at 11[14].

According to Malaysian CPG for breast cancer, increased breast density is another risk factor for breast cancer. It increases 2 times the risk in fibro-glandular density and up to 4 times in extremely dense breast[15]. A study conducted by the Canadian national breast screening study showed that there was a 43% increase in the relative risk (RR) between the lower and the next higher category of density while Normal et al suggest that women with density in 75% or more had an increased risk of breast cancer (odds ratio, 4.7) as compared with women with density in less than 10% of the mammogram. [16,17]

As for the non-modifiable risk factor, reproductive factor plays a major role. Li et at has found out that nulliparity increase the risk up to 1.26 times[12]. Similar findings was found by Kelsey et al as they found out that nulliparous women are at increased risk for breast cancer compared with parous women (RR from 1.2 to 1.7)[18]. Meanwhile, the effect of parity differs depending upon the age of first birth. In the Nurses' Health Study, when compared with nulliparous women, the cumulative incidence of breast cancer was 20 percent lower, 10 percent

lower, and 5 percent higher among women who delivered their first child at age 20, 25, or 35 years, respectively[19].

Other than that, hormonal factor also can leads to breast cancer. It was found out that the use of oral contraceptives pills can increase the risk of breast cancer up to 1.52 times[20]. A study by the Norwegian Women and Cancer Study showed that the use of progestin only pills more than 5 years were associated with increase in ER + breast cancer[21].

In addition to those mentioned above, history of radiation to the chest might as well increase the risk of breast cancer. A study to a group of patient who had history of childhood radiation that were treated with lower delivered doses of radiation to a large volume had a high risk of breast cancer (standardized incidence ratio [SIR], 43.6 as did survivors treated with high doses of delivered radiation to the mantle field (SIR, 24.2; 95% CI, 20.7 to 28.3)[22].

One factor that might have a role to reduce the risk of breast cancer is breastfeeding. A large pooled analysis that included individual data from 47 epidemiologic studies (50,302 women with invasive breast cancer and 96,973 controls) estimated that for every 12 months of breastfeeding, there was a 4.3 percent reduction in the relative risk (RR) of breast cancer[23]. Another meta-analysis suggested that this association was stronger for hormone receptor-negative breast cancers[24]. However, a systemic review by Li yang et al, suggest that no consensus about the relationship about the relationship of breast feeding and breast cancer as they only found out that of the 24 studies of the effect of breastfeeding duration, only 13 found a reduced risk of breast cancer with extended lactation[25].

Another important factor that plays a role in breast cancer development is patient personal lifestyles for example exercise, alcohol intake, smoking and obesity. Slattery et al noted that among premenopausal women, high total metabolic equivalent of the task (MET) hours of activity during the referent year was associated with reduced breast cancer risk (odds

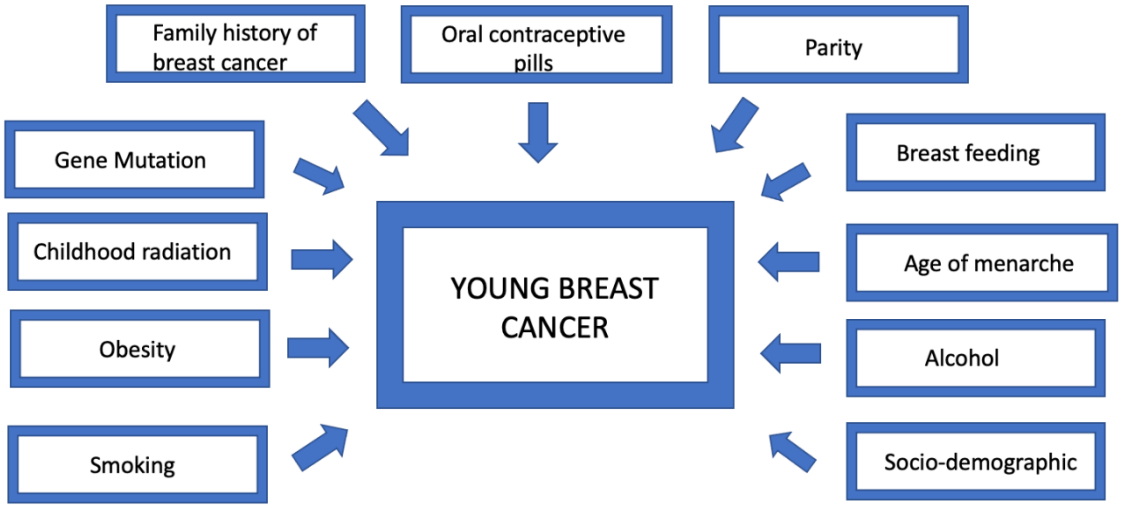
ratio 0.62)[26].Systematic review by Friedenreich et al also shows that increased physical activity reduced the risk about 25-30 %[27].

Smoking was well known to increase the risk of breast cancer. A prospective study by Inger et al concluded that women who had smoked for more than 20 pack-years and initiated smoking more than 5 years before their first childbirth had an overall risk of breast cancer that was 35% higher[28]. Another study also suggests that even if a woman is a passive smoker, the risk increased. This meta-analysis showed that of 11 prospective studies, the SRR for breast cancer was 1.07 with no heterogeneity[29].

As for alcohol, it is not only associated with the increase risk of breast cancer, but also other system as well for example pharyngeal, oesophageal and colorectal cancer[30]. For breast cancer, there is increase of relative risk by 1.61[30]. This is also supported by a meta-analysis done in 2013 which showed a small but significant association between female breast cancer and light alcohol intake (RR 1.05)[31].

Interesting findings was found with regards of obesity. A higher BMI and/or perimenopausal weight gain have been consistently associated with a higher risk of breast cancer among postmenopausal women[32].However, unlike post-menopausal women, an increased BMI is associated with a **lower** risk of breast cancer in premenopausal women. In a multi-center analysis using pooled individual-level data from approximately 760,000 premenopausal women from 19 prospective cohorts, there was a 4.2-fold increased risk between the highest and lowest BMI categories[33].

Conceptual framework



The risk factors that leads to development of Young breast cancer

Objectives

General objectives

1. To determine the risk factors of young breast cancer between year 2015 to 2021 in Pulau Pinang and Kelantan

Specific objectives

1. To determine the socio-demography of young breast cancer between year 2015 to 2021 in Pulau Pinang and Kelantan
2. To evaluate clinicopathological data of young breast cancer between year 2015 to 2021 in Pulau Pinang and Kelantan

3. To determine the risk factors of young breast cancer between year 2015 to 2021 in Pulau Pinang and Kelantan

4.

Research question

1. What are the risk factors for young breast cancer?

Hypothesis

The significant risk factor in young breast cancer are family history of breast cancer, oral contraceptive pills, breastfeeding, gene mutation, early menarche, numbers of parity, obesity, history of chest radiation, alcohol intake and smoking.

Methodology

Research design

This is a retrospective case control study

Study venue

Hospital Seberang Jaya, Hospital Pulau Pinang, Hospital Univerisiti Sains Malaysia & Institut Perubatan dan Pergigian Termaju.

Study duration

January 2021 – December 2022

Study population

REFERENCE POPULATION

Breast cancer patient less than 40 years old in Pulau Pinang and Kelantan

TARGET POPULATION

Breast cancer patient less than 40 years old that attend breast clinic in Hospital Pulau Pinang, Hospital Seberang Jaya, Hospital Universiti Sains Malaysia and Institut Perubatan & Pergigian Termaju.

SOURCE POPULATION

Breast cancer patient less than 40 years old that attend breast clinic in Hospital Pulau Pinang, Hospital Seberang Jaya, Hospital Universiti Sains Malaysia and Institut Perubatan & Pergigian Termaju.

SAMPLING FRAME

Patients' medical records from breast clinic in Hospital Pulau Pinang, Hospital Seberang Jaya, Hospital Universiti Sains Malaysia and Institut Perubatan & Pergigian Termaju that fulfil the inclusion and exclusion criteria of both case and control from January 2015 to December 2021.

Sample size

Reference : Essiban et al (year 2020)

Using double proportion formula

Two proportions:

$$n = \frac{p_1(1-p_1) + p_2(1-p_2)}{(p_1 - p_2)^2}(z_\alpha + z_\beta)^2$$

n= sample size

p1= the probability of exposure in cases

p2= the probability of exposure in controls

Zα = 1.96 for α= 0.05 (two tailed)

Zβ = 0.84 for 80% power

Highest sample size based on oral contraceptive pills as risk factor

p1: 0.62

p2: 0.44

n : 120 (per arm) + 10 % dropout

: 133 per arm

Selection criteria

Case

Inclusion criteria

1. Patient diagnosed with breast cancer at age less than 40 years old. Diagnosis made via triple assessment (physical examination, imaging, and biopsy)
2. Patient with complete socio-demographic and clinicopathological data.
3. Patient with clinical staging done.

Exclusion criteria

1. Male patient
2. Patient less than 18 years old

Control

Inclusion criteria

1.Patients with breast symptoms at age less than 40 years old

2.Patient with complete socio-demographic and clinicopathological data

3.Patient underwent breast imaging (ultrasound of breast)

4.Histopathological evidence negatives of breast cancer.

Exclusion criteria

1. Male patient
2. Patient less than 18 years old

Sampling method

Sampling for CASE

The archives data(clinic notes, operative notes) from Cluster Seberang Jaya Hospital (Hospital Seberang Jaya, Hospital Kepala Batas, Hospital Bukit Mertajam, Hospital Sungai Bakap),Pulau Pinang General Hospital, Hospital Univerisiti Sains Malaysia and Institut Perubatan dan Pergigian Termaju will be reviewed.

All patient less than 40 years old attending breast clinic in the above mentioned hospital from January 2015 till December 2021 which fulfil the inclusion and exclusion criteria of the study 'case' will be be included in the study.

Sampling of CONTROL

The archives data(clinic notes, operative notes) from Cluster Seberang Jaya Hospital (Hospital Seberang Jaya, Hospital Kepala Batas, Hospital Bukit Mertajam, Hospital Sungai Bakap), Pulau Pinang General Hospital Hospital Univerisiti Sains Malaysia and Institut Perubatan dan Pergigian Termaju will be reviewed.

All patient less than 40 years old attending breast clinic in the above mentioned hospital from January 2015 until December 2021 which fulfil the inclusion and exclusion criteria of the study 'control' will be be included in the study.

This is a case-control study. Once the minimum number of both case and control is achieved, the recruitment will stop.

Research tools and data collection

Data collection will be taken from Surgical Outpatient Department (SOPD) records.

The demographics, risk factors and clinic-pathological data will be collected in the data collection proforma.

Operational definition

Young breast cancer	Cancer that developed less than 40 years old
HPP	Hospital Pulau Pinang
HSJ	Hospital Seberang Jaya
Obesity	Body mass index >30
OCP	Oral contraceptive pills
BIRADS	Breast imaging-reporting data system

Data Analysis

All data will be analysed using SPSS version 26.

Descriptive statistics will be used to summarise the socio-demographic characteristics of patients.

Continuous data will be summarised as mean (standard deviation (SD)) or median (interquartile range (IQR)) depending upon the normality of distribution, whereas categorical data will be presented as frequency (percentage (%)).

Inferential analysis will be used using Independent t-test, Paired t test, Pearson Chi-Square/ Fisher exact test for suitable data e.g., numerical and categorical.

The Independent t-test used to determine the comparison of means between two unrelated groups on the same continuous, dependent variable.

The Paired t-test used to determine the difference between two variables for the same subjects. Meanwhile, the Pearson Chi-Square used to identify the association between two categorical variables, and Fisher Exact test useful for 2x2 tables.

Simple logistic regression used to predict the predicts the probability that an observation falls into one of two categories of a dichotomous dependent variable based on one or more independent variables that can be either continuous or categorical

Multiple logistic regression will be used to identify the factors associated with development of young breast cancer.

Results will be presented as odd ratios (OR), 95% confidence interval (CI) and p value. The p value <0.05 will be considered to indicate statistical significance.

Expected result

Variables	Cases n(%)	Control n(%)	Odds ratio (OR)	P-value
Family history of breast malignancy				
Known gene mutation				
Age of menarche				
Parity				
Breast feeding				

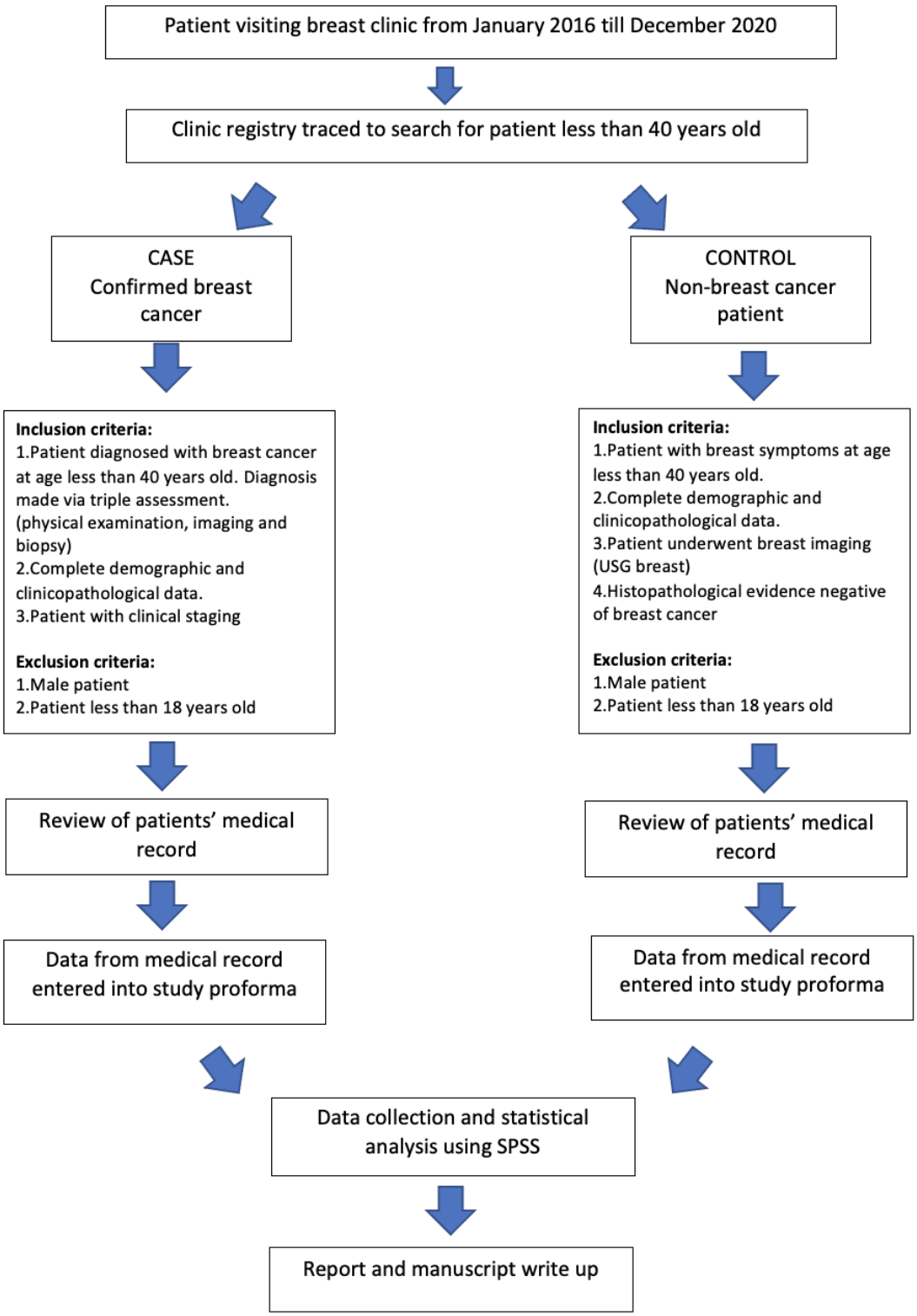
Oral contraceptive pills				
History of chest radiation				
Obesity				
Smoking				
Alcohol Intake				

Ethical approval

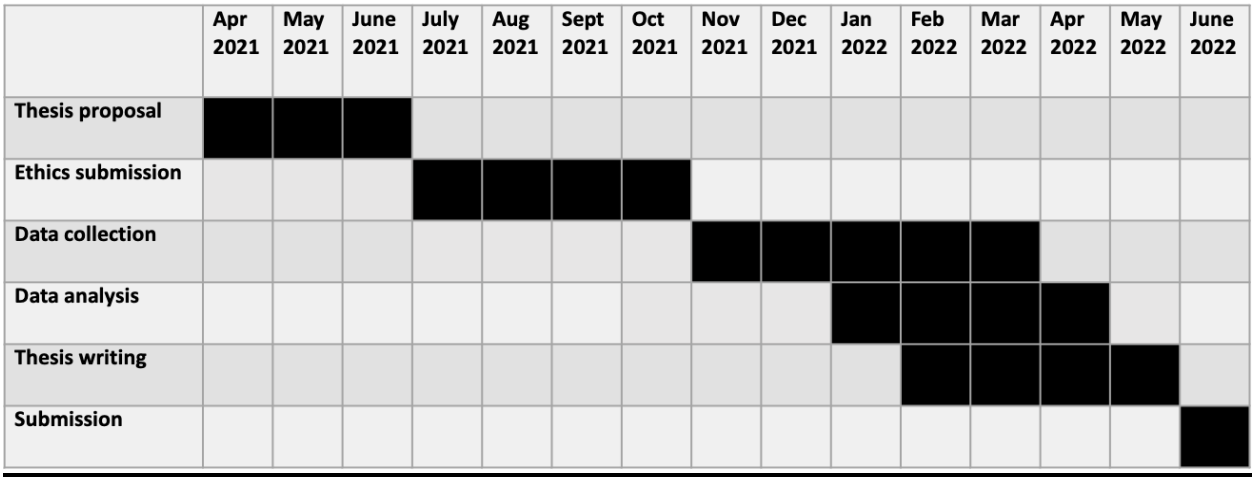
Ethical approval is will be applied before conducting the study from University Sains Malaysia Ethical Committee and Kementerian Kesihatan Malaysia. No tissue or body fluid needed as only existing data is extracted for analysis.

Consent not applicable in this study

Flow chart


Patient visiting breast clinic from January 2016 till December 2020
Clinic registry traced to search for patient less than 40 years old
CASE
Confirmed breast cancer
CONTROL
Non-breast cancer patient
Inclusion criteria:
1.Patient diagnosed with breast cancer at age less than 40 years old. Diagnosis made via triple assessment. (physical examination, imaging and biopsy)
2.Complete demographic and clinicopathological data.
3.Patient with clinical staging
Exclusion criteria:
1.Male patient
2.Patient less than 18 years old
Inclusion criteria:
1.Patient with breast symptoms at age less than 40 years old.
2.Complete demographic and clinicopathological data.
3.Patient underwent breast imaging (USG breast)
4.Histopathological evidence negative of breast cancer
Exclusion criteria:
1.Male patient
2.Patient less than 18 years old
Review of patients' medical record
Review of patients' medical record
Data from medical record entered into study proforma
Data from medical record entered into study proforma
Data collection and statistical analysis using SPSS
Report and manuscript write up

Gantt chart



Planned milestones

May 2021 - Proposal completion and presentation

November 2021 - Ethics committee approval

April 2022 - Completion of data collection and analysis

May 2022 - Thesis writing completion

June 2022 - Submission

Budget

Self-funding

1. Printing cost of questionnaire, 5 pages each set.

5 pages x 5cent/page x 200sets = RM 50

2. Miscellaneous, example: additional papers, pens, organising folders, storage box.

Estimation: RM50

3. Hard cover for thesis

4 hard cover copies x RM 100 = RM 400

Total estimation cost: RM 500

ATTACHMENT

UNIVERSITI SAINS MALAYSIA

(PROFORMA)

No .

TITLE: RISK FACTOR OF YOUNG BREAST CANCER IN PULAU PINANG

DEMOGRAPHIC DETAILS

Identification Card number :

Date of birth :

Date of diagnosis :

Age at diagnosis (confirmed by pathology) :

Ethnicity

☐ Malay ☐ Chinese ☐ Indian ☐ Others _____

Educational Level :

☐ Primary ☐ Secondary ☐ University

HISTORY

Date of presentation (at first contact): _____

Mode of initial presentation:

☐ Breast lump ☐ Pain (mastalgia)

☐ Nipple discharge ☐ Others (please specify): _____

Duration of noticing:

☐ < 1 months ☐ 2-4 months ☐ 5-8 months ☐ 9-12 month ☐ > 1 year

Underlying other malignancy: ☐ Yes ☐ No

If yes, what malignancy and when? _____

Family history of breast malignancy: ☐ Yes ☐ No

If yes, age of diagnosis: _____ years old

If there is a family history of breast malignancy, who are they related to?

☐ First degree (parents, siblings, children)

☐ Second degree (grandparents, aunts or uncles, nieces or nephews, grandchildren)

☐ Third degree (first cousin)

Known gene mutation: ☐ Yes ☐ No

If yes, please specify:

☐ BRCA ☐ TP53 ☐ others: _____

Family history of other malignancy: ☐ Yes ☐ No

If yes, what type of malignancy and relationship. _____

Age of menarche: _____ years old

Parity: _____ **Age of first livebirth**: _____ years old

Breast feeding: ☐ Yes ☐ No

If yes, duration: _____ months/years

Oral contraceptive pills: ☐ Yes ☐ No

If yes, duration: _____months/years

Types of contraceptive pills: _____

History of chest radiation in childhood: ☐ Yes ☐ No

Comorbidities: Diabetes**/** Hypertension**/** Renal Failure**/** Heart disease **/**Asthma/ others

Obesity: ☐ Yes ☐ No

Alcohol intake: ☐ Yes ☐ No

Smoking: ☐ Yes ☐ No

CLINICAL EXAMINATION

Assessment of the tumor:

Side: ☐ Right ☐ Left

Site:

☐ Upper outer quadrant ☐ Upper inner quadrant

☐ Lower outer quadrant ☐ Lower inner quadrant

☐ Central

Fixation:

☐ No

☐ Yes (T4)

(If Yes, skip the Size and proceed with the Assessment of Lymph Nodes)

Size:

Size: ____cm	Tumor (T)	Explanation
☐	TX	Primary tumor cannot be assessed
☐	T0	No evidence of primary tumor

☐	Tis	Carcinoma in situ
☐	T1	Tumor ≤2cm in greatest dimension
☐	T2	Tumor >2cm but ≤5cm in greatest dimension
☐	T3	Tumor >5cm in greatest dimension
☐	T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodule)

Assessment of Lymph Nodes:

	Node	Explanation
☐	NX	Regional lymph nodes cannot be assessed (e.g.: previously removed)
☐	N0	No regional lymph node metastases
☐	N1	Metastases to movable ipsilateral axillary lymph node(s)
☐ ☐	N2	Metastases in ipsilateral axillary lymph node that are clinically fixed or matted; OR Clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node
☐ ☐ ☐	N3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; OR Clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; OR Metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

<u>INVESTIGATION</u>

Ultrasound breast (BIRADS CLASSIFICATION-Breast density)

☐ Class A ☐ Class B ☐ Class C ☐ Class D

Mammogram

☐ BIRADS 1 ☐ BIRADS 2 ☐ BIRADS 3 ☐ BIRADS 4 ☐ BIRADS 5 ☐ BIRADS 6

Staging investigation:

☐ CT scan ☐ Bone scan ☐ PET scan

☐ MRI ☐ Ultrasound abdomen

Any evidence of metastasis? ☐ Yes (M1) ☐ No (M0)

Final Clinical Staging (TNM): _____

☐	Stage 0	Tis	N0	M0
☐	Stage IA	T1	N0	M0
	Stage IB	T0	N1mi	M0
		T1	N1mi	M0
☐	Stage IIA	T0	N1	M0
		T1	N1	M0
		T2	N0	M0
	Stage IIb	T2	N1	M0
		T3	N0	M0
☐	Stage IIIA	T0	N2	M0
		T1	N2	M0
		T2	N2	M0
		T3	N1	M0
		T3	N2	M0
	Stage IIIB	T4	N0	M0
		T4	N1	M0
		T4	N2	M0
	Stage IIIC	Any T	N3	M0
☐	Stage IV	Any T	Any N	M1

TREATMENT

Neoadjuvant chemotherapy: ☐ Yes ☐ No

Surgery:

☐ Breast Conserving Surgery (BCS) with Axillary dissection

☐ Mastectomy with Axillary Clearance

PATHOLOGY

Histology type:

☐ Infiltrating Ductal Carcinoma (IDC) NOS ☐ Lobular Carcinoma In Situ (LCIS)

☐ Infiltrating Lobular Carcinoma (ILC) ☐ Medullary

☐ Ductal Carcinoma In Situ (DCIS) ☐ Others (please specify):

_____

Histological Grading (Bloom-Richardson grading system):