RATE OF WEIGHT GAIN AND ITS ASSOCIATION WITH HOMEOSTATIC MODEL ASSESSMENT-INSULIN RESISTANCE (HOMA-IR) AMONG OBESE CHILDREN ATTENDING PEDIATRIC ENDOCRINE CLINIC HOSPITAL UNIVERSITI SAINS MALAYSIA

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER IN MEDICINE (PAEDIATRICS)

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Acknowledgement

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LIST OF TABLES AND FIGURES

LIST OF ABBREBIATION AND NOMENCLATURE

HUSM : Hospital Universiti Sains Malaysia

HOMA-IR : Hemostasis Model Assessment-Insulin Resistance

IR : Insulin Resistance

BMI : Body Mass Index

IFG : Impaired Fasting Glucose

IGT : Impaired Glucose Tolerance

T2DM : Type 2 Diabetes Mellitus

MOGTT : Modified Oral Glucose Tolerance Test

FLP : Fasting lipid profile

FBS : Fasting blood sugar

CI : Confidence Interval

OR : Odd Ratio

HR : Hazard Ratio

SD : Standard deviation

IQR : Interquartile range

NAFLD : Nonalcoholic fatty liver disease

WC : Waist circumference

ABSTRAK

Objektif : Mengkaji masa median kenaikan berat badan dari berat asal, factor-faktor yang mempengaruhi kadar kenaikan berat dan hubungan antara berat badan dan Penilaian Model Homesostasis-Rintangan Insulin di kalangan pesakit obesiti yang menghadiri Klinik Endokrin Hospital Universiti Sains Malaysia.

Kaedah: Kami telah mengumpulkan 70 peserta berumur 1-18 tahun, primari obesiti yang memenuhi kriteria pilihan. Kami telah menganalisa demografik mereka (umur, jantina, etnik , latar belakang keluarga), mengambil bacaan antropometri (berat , tinggi , index jisim tubuh), memantau kenaikan berat bulanan dan menganalisa bacaan Penilaian Model Homesostasis-Rintangan Insulin mereka pada perjumpaan pertama dan 6 bulan kemudian.

Keputusan: Masa median untuk pertambahan 5kg berat dari berat asal adalah 16 minggu (98% CI): (15.2,16.7). Analisa multivarit menunjukkan hanya HOMA-IR ketika 6 bulan boleh mempengaruhi penambahan 5kg berat Adjusted HR: (95%CI) 1.617(1.232, 2.123), (p=0.001).

Kesimpulan: Masa untuk pertambahan 5kg berat dari berat asal akan meningkat 1.6 kali ganda dengan kehadiran rintangan insulin pada 6 bulan temujanji bagi pesakit obesiti.

Kata Kunci: Penilaian Homesostatis-Rintangan Insulin, faktor prognostik, masa median

ABSTRACT

Objective: We aimed to study the median time to gain weight from the baseline, the factors that influences the rate of weight gain and correlation between weight gain and Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) among obese children attending pediatric endocrine clinic Hospital USM.

Method: This was a prospective cohort study. No sampling method was applied, all eligible patient were included in the study. We recruited 70 participants, aged from 1-18 years old, primary obesity that full filled inclusion criteria from June 2019 until September 2020. We analysed their demography (age, gender, ethnicity, family background) using questionnaire, measured their anthropometry (weight, height, BMI) and monitor monthly weight increment and finally analysed their HOMA-IR at baseline and 6 months follow up.

Results: The mean time to gain 5kg from the baseline was 16weeks (98% CI): (15.2,16.7). Multivariate analysis showed only HOMA-IR after 6 months was a significant predictor affecting time to gain 5kg; Adjusted HR: (95%CI) 1.617(1.232, 2.123), (p=0.001).

Conclusion: The time to gain 5kg from the baseline was increased 1.6 times in the presence of insulin resistance at 6 months follow up in patient with obesity.

Keyword: *HOMA-IR, prognostic factor, mean time.*

CHAPTER II

THE TEXT

2.1 Section A:

Introduction

Introduction

Obesity in children and adolescence has become a massive health problem in many countries. Childhood obesity, especially in developed countries, has increased dramatically in the last 20 years.[1] The WHO stated Americas and eastern Mediterranean regions had higher prevalence of overweight and obesity (30-40%) than European (20-30%), south-east Asian, western Pacific, and African regions (10-20% in the latter three).[2]

The worldwide prevalence of childhood overweight and obese increased from 4.2% (95% CI: 3.2%, 5.2%) in 1990 to 6.7% (95% CI: 5.6%, 7.7%) in 2010.[3] This had reach 9.1% (95% CI:7.3%,10.6%) or 60 million in 2020. The prevalence of obesity was lower in Asia (4.9% in 2010) than in Africa (8.5% in 2010) but the numbers of affected children (18 million) was higher in Asia.[3]

The problem of childhood obesity was global and extends into the developing world, in Thailand the prevalence of obesity in 5-12 years old children increased from 12.2% to 15.6% within two years (WHO, 2003). The National Health and Morbidity survey (NHMS) by Institute of Public Heath ,2015 reported that the prevalence of obesity among children aged 10-14 years in Malaysia was 14.4%

Obesity is caused by an imbalance in energy input versus output, resulting in a positive energy balance. The International Obesity Task Force develop an international standard BMI for age, in which the 85^{th} percentile and the 95^{th} percentile for are roughly correspond to BMI of $25kg/m^2$ and $30kg/m^2$ respectively in 18 years old.[4]

Childhood obesity is associated with an increased risk for several metabolic complications, such as insulin resistance, glucose intolerance and type 2 diabetes mellitus (T2DM). In particular, insulin resistance is the most common metabolic alteration related to obesity, it represents an important link between obesity and other metabolic as well as cardiovascular complications.

Insulin Resistance (IR) is defined as a condition in which plasma insulin at normal concentration has an impaired ability to adequately promote peripheral glucose disposal, hepatic glucose suppression and inhibition of very low-density lipoprotein output.[5] In case of IR, insulin production by the pancreatic β-cell is increased, causing hyperinsulinemia. Failure of the compensatory response leads impaired glucose tolerance and eventually T2DM.

The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is the most commonly used method in daily practice and a way to measure insulin resistance in children.[6] It is used to yield an estimate of insulin sensitivity and β-cell function from fasting plasma insulin and glucose concentration. The HOMA value was calculated as follow – fasting insulin(mU/L) x fasting glucose(nmol/L)/22.5 (using HOMA calculator version 2.2).[6]

According to study by Consuela Chang-Rueda *et al* (2018); Correlation of HOMA-IR with BMI for age percentile in children and adolescence, they concluded that HOMA-IR had a moderately significant correlation with an increase in BMI percentile (r=0.198, p=0.037) .[7] The HOMA-IR values correlated positively with age (r=0,.636) weight (r=0.569),

height (r=0.578) and BMI percentile (r=0.198).

A large prospective cohort study by Peplies *et al* (2016) was the first prospective study on IR in a preadolescent children's population.[8] The study showed the strongest positive association of IR were BMI z score , waist circumference z score , audio-visual media time ; and an inverse association with determined physical activity . A longitudinal reduction of HOMA-IR was accompanied with a parallel reduction of BMI. This study supported the common hypothesis that overweight and obesity were the main determinants of IR. Their data also indicate that physical activity and a sedentary lifestyle was likewise associated with the development of IR, independent of weight status.

Insulin resistance syndrome was the most common co morbid for obesity in many clinical trials. It was found that the higher weight or body mass index (BMI), the more risk to get insulin resistance syndrome. As far as we know, there is no study that particularly shows correlate between rate of weight gain and insulin resistance syndrome in children. Therefore, the main purpose of this study is to investigate whether the rate of weight gain contribute to development of insulin resistance syndrome.

2.1 Section B

Study protocol

2.2.1 Documents submitted for ethical approval

RATE OF WEIGHT GAIN AND ITS ASSOCIATION WITH HOMEOSTATIC MODEL ASSESSMENT-INSULIN RESISTANCE (HOMA-IR) AMONG OBESE CHILDREN ATTENDING PEDIATRIC ENDOCRINE CLINIC HOSPITAL UNIVERSITI SAINS MALAYSIA

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2020

Research title:

Rate of weight gain and its association with Homeostatic Model Assessment-Insulin Resitance (HOMA -IR) among obese children attending pediatric endocrine clinic Hospital Universiti Sains Malaysia.

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1.0 Introduction

Obesity in children and adolescence has become a massive health problem in many countries. Childhood obesity, especially in developed countries, has increased dramatically in the last 20 years.[1] The National Health and Morbidity survey (NHMS) 2015 reported that the prevalence of obesity among children aged 10-14 years in Malaysia was 14.4% (IPH,2015).

The increasing prevalence of obesity in children and adolescence worldwide may have alarming consequences in term of future morbidities. Traditional approaches for the management of overweight and obesity had poor long-term efficacy and therefore prevention is currently the most promising strategy for controlling the obesity epidemic.

The early metabolic consequence of obesity is disturbance of glucose and insulin homeostatic.[2] Hence, one of the metabolic complications observed among the overweight or obese children is insulin resistance (van der Aa *et al*.,2015). Insulin resistance is defined as a condition in which plasma insulin at normal concentration has an impaired ability to adequately promote peripheral glucose disposal, hepatic glucose suppression and inhibition of very low-density lipoprotein output.[3]

The Homeostatic model assessment-Insulin Resistance (HOMA) is a way to measure insulin resistance in children.[4] It is used to yield an estimate of insulin sensitivity and β-cell function from fasting plasma insulin and glucose concentration. The HOMA value was calculated as follow – fasting insulin(mU/L) x fasting glucose(nmol/L)/22.5 (using HOMA calculator version 2.2).[6]

In HUSM, they have paediatric endocrine clinic that received referral for paediatric obesity up to the age 18 years old. The services that offer are recognition of obesity by doing history taking and examination to differentiate exogenous or endogenous cause of obesity, treatment and management of obesity. Routinely, they send blood investigations for Fasting lipid profiles, triglycerides, total cholesterol, high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL), fasting blood glucose, and insulin level. Thyroid function test, liver function test and renal functions test are also assessed. Oral glucose tolerance test (OGTT) will be performed for all patients as they are at risk of diabetes. All the blood parameter taken is a part of standard and routine investigation at the paediatric endocrine clinic. The detailed dietary clerking also be done by endocrine team at the clinic because the main management is still lifestyle modification. As a researcher, I will collect the data from the notes and there will be no extra blood taking, everything is part of routine service.

2.0 Problem statement & Study rationale

There are many studies that conclude, the most common co morbid for obesity is insulin resistance syndrome. It was found that the higher weight or body mass index (BMI), the more risk to get insulin resistance syndrome. The insulin resistance was measured using Homeostasis Model Assessment-Insulin Resistance (HOMA-IR). As far as we know, there is no study that particularly correlates between rate of weight gain and insulin resistance syndrome in children. Therefore, the main purpose of this study is to investigate whether the rate of weight gain contribute to insulin resistance syndrome or not.

3.0 What is the use of your study finding?

1. To study median time to gain weight from the baseline and the factor that influences the rate of weight gain.
2. To find correlation between weight gain and Homeostatic Model Assessment (HOMA-IR).

4.0 Literature review

Insulin sensitivity and secretion in normal children related to size at birth, postnatal growth and plasma insulin-like growth factor I levels by *K. K. Ong, C. J.Petry. P.M Emmet. M.sandhu. W.Kiess. C.N. hales.A.R.Ness. D.B. dunger, the ALSPAC study team.*

This study determined the association between early postnatal variation in height, weight gain and IGF-I with risk for adult disease. A prospective birth cohort study was conducted among 851 normal 8-year-old children. They measured the fasting insulin sensitivity (%HOMA) and insulin secretion post oral glucose (insulinogenic index 0-30 min). They also examined the association between size at birth, postnatal weight gain, and circulating IGF-I level with insulin sensitivity and secretion at 8 years old.

The outcomes of the study were fasting insulin sensitivity at 8 years closely related

to current BMI (r=0.33, p<0.0005) and the lower insulin sensitivity with higher BMI and waist circumference were all predicted by greater weight gain between birth to 3 years old (all p <0.0005). The conclusion from the study was the insulin resistance dependent on rapid weight gain during the early postnatal life.

Longitudinal changes in insulin sensitivity and secretion from birth to 3 years in small and appropriate for gestational age children by *V.Mericq. K.K.ong. R.Bazaes.VPena.A.Avila. T Salazar. N Soto. G Iniquiez. D.B Dunger.*

They studied the risk of insulin resistance and type 2 diabetes in human subjects who were small for gestational age (SGA)at birth as a consequences of rapid early postnatal weight gain. It was a prospective study, conducted from birth to 3-year-old age in 55 SGA newborn and 13 with birth weight appropriate for gestational age (AGA).

Weight and height was measured at birth, and age 1, 2 and 3 years. 48 hours after birth, a pre feeding 3ml blood sample was obtained for determination of glucose, insulin and other marker of insulin sensitivity and secretion. Subsequently, a short IV glucose tolerance test that was conducted at 1and 3year old and the insulin resistance were measured using HOMA-IR formula. Results were fasting insulin resistance (HOMA-IR) at 3 years related to weight gain between 0-3 years in infants with AGA and SGA (r=0.47, p=0.0003). The other outcome was SGA infant had lower pre feed insulin levels at postnatal age 48 h than AGA(median 38.9 vs 23.8pmol/l , p < 0.005, but higher fasting insulin level at 3-year-old (median 38.9 vs 23.8 pmol/L , p<0.0050, in which related to rate of weight gain between 0-3 years (r=0.47, p=0.0003).

The conclusion were SGA infants showed a marked transition from lower pre feed insulin and increased insulin sensitivity at birth to insulin resistance over the first 3 years of life.

Early Development of adiposity and Insulin Resistance after catch up Weight gain in Small for Gestational Age Children by *Lourdes Ibanez, Ken Ong, David B. Dunger and Francis de Zegher. JCEM 2006.*

They studied the association between low birth weight followed by rapid postnatal weight gain with long term risk for central obesity and insulin resistance. It was a longitudinal cohort study in low birth weight (SGA; n= 29) and normal birth weight (AGA; n=22_ childrens from Barcelona. They measured the body composition by dual energy Xray absorptiometry scan, and assessed insulin sensitivity (using HOMA) longitudinally at aged 2, 3 and 4 years.

The outcome was SGA children had greater adiposity, insulin resistance and higher neutrophil count than AGA (p=0.01-0.0004). In SGA children, total and abdominal fat mass at 4 years was closely related to rate of weight gain between 0-2 years (p=0.002-0.0003) than between 2-4 years (p=0.04-0.1). The conclusion was SGA children showed a dramatic transition toward central adiposity and insulin resistance between 2-4 years as a consequent to catch up weight gain between birth and 2 year.

Insulin resistance and its association with catch up growth in Chinese children born small for gestational age by *Chunhualiu, Baiyan WU, Niyang Lin and Xiaoyi Fang.*

This study was to assess the insulin resistance and β-cell function from birth to 4 years and to examine their association with catch up growth (CUG) in Chinese small gestational age (SGA) children. It was a case control study consisted of 145 children who were born either SGA (n=70) or AGA (n=75) from birth to 4 years of age. Weight and height were measured yearly from birth to age 4 years and transformed into age-and gender –adjusted SD score. Fasting serum insulin and glucose were measured, and fasting insulin resistance and β-cell

function were estimated using homeostasis model assessment (HOMA).

The results from this study showed that the HOMA % was significantly correlated with the weight gain with SD of weight gain between 6-12 months (r=0.636, p=0.01 and r=0.572, p=0.01). The conclusion was SGA children with catch up growth show a greater propensity to develop insulin resistance than AGA children between 2-4 years old. HOMA parameter was related to catch up growth in first year of life.

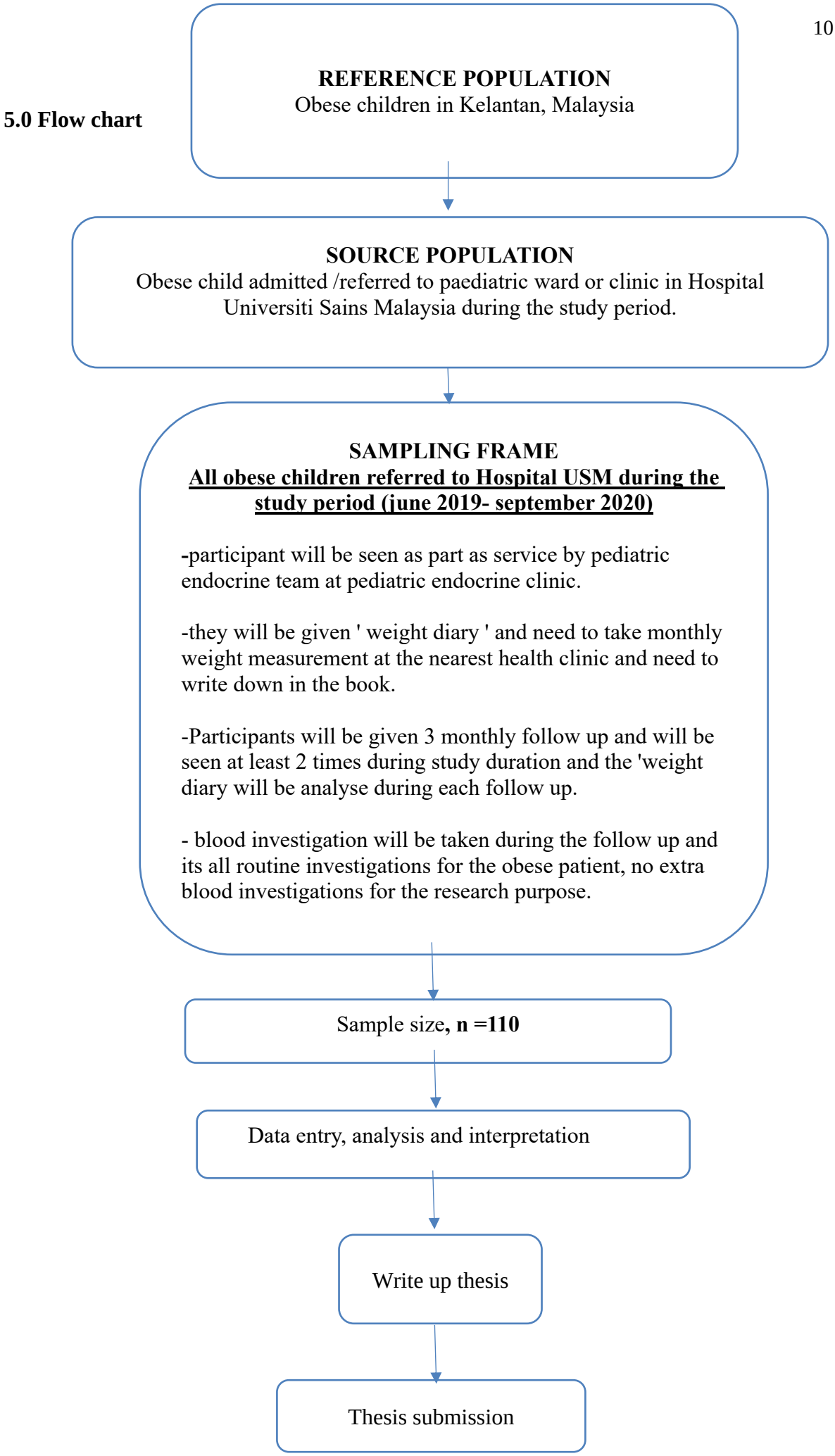
Activity, Dietary Intake, Weight Changes in a Longitudinal Study of Preadolescent and Adolescence Boys and Girls by *Catherine S. Berkey, HelaineR.H .Rockett, MS , RD, Alison E, Field, ScD, Matthew W, Gillman,MD, SM, A.Lindsay Frazier, Carlos A. Camargo, Graham A. Colditz.*

This study was to determine the role of physical activity, inactivity, dietary pattern on annual weight changes amount preadolescence and adolecence, taking growth and development into account. It was a cohort study of girl (n = 8980) and boy (n =7791), aged 9 till 14 years old. The regression analysis of 1 year change in BMI among boys and girl were used.

Result of annual BMI was increased in girl with higher calories intake (BMI increased by 0.0061kg/m2 per 100kcal/day , $p< 0.02$, more spent time on TV/video(BMI increased by 0.372kg /m2/h; $p<0.001$), and less physical activity (BMI decreased 0.0284kg/m2/hour/day of activity ;$p<0.05$) .Boys spent more time on TV/ video/games (0.0384kg/m2/daily hour;$p<0.0001$, and less physical activity ($p<0.094$) incresaed annual BMI measurement within 2 years. However, calories intake had no significant association changes in BMI among boys. ($p>0.10$).

As a conclusion, both boys and girls increased in 1 year BMI among those who spent more time with TV/videos/games and les physcial activity.

5.0 Flow chart



6.0 Target Research Question(s)

The time to gain 1, 3 and 5kg weight from the baseline and the correlation between the rate of weight gain and Homeostasis Model Assessment (HOMA-IR). The values were chosen as the guidelines stated weight reduction is between 0.5kg-1.0kg a month.[5]

7.0 Objective

General

To study time to gain 1,3, 5kg weight and correlation between rate of weight gain with HOMA-IR among obese children.

Primary objective

a. To study median time to gain 1, 3 and 5kg weight from the baseline weight.

b. To determine the factors that influence the time to gain weight from its baseline.

Secondary objective

a.To study between weight gain and its association with HOMA-IR among obese patient.

8.0 Research study

Prospective cohort study

9.0 Hypothesis

a. Age, gender, dietary pattern, sedentary lifestyle and socioeconomic status of the family are significant factors for time to gain weight.
b. There is significant correlation between rapid weight gains with HOMA-IR.

10.0 Study area

Paediatric ward (inpatient) and clinic (outpatient) Hospital Universiti Sains Malaysia Kubang Kerian, Kota Bharu, Kelantan Darul Naim.

11.0 Study period

1 year 3 months (June 2019-September 2020)

12.0 Study population

Patient who are admitted or referred to Paediatric ward and clinic. Those patients who fulfill the inclusion criteria will be included in the study.

Reference population	Obese Children in Kelantan
Source population	Obese children in Kelantan
Target population	Obese patient who are admitted or referred and follow up in Paediatric Endocrine clinic HUSM.
Sampling frame	Obese patient who are admitted or referred and follow up in Pediatric Endocrine clinic HUSM.

All obese children who are admitted or referred to paediatric ward and clinic in HUSM. The participant will be given 3 monthly follow up and they will be seen at least 2 times during study period.

Inclusion criteria:

1. All obese children
2. Primary/simple obesity
3. Waist Circumference > 90^{th} percentile according to WHO waist circumference chart.
4. BMI> 95th centile according to WHO BMI chart.

Exclusion criteria:

1. Patient with secondary causes of obesity such as monogenic disorder, syndromes,

neurologic, endocrine, drug induced and hypothalamic causes.

2. Patient who defaulted follow up and not compliant to monthly weight measurement.

14.0 Sample size estimation

Primary objective:

Primary objective is calculated using PS software (survival analysis) .No prior study reported time to gain weight from the baseline, however based on expert opinion, increase of 5kg weight on average is 6 months.

a= 0.05, power=0.8, A=12 month, F=3/12, m=1

m1: 6/12(time for female to gain >5kg)

m2: 3/12 (time for male to gain >5kg)

n=46 x 2 =92 patients

added 20% dropout **n =110 patients**

Secondary objective:

For secondary objective are calculated by using sample size G Power software (sample size for survival analysis).

r= 0.3, a= 0.05, power =0.8

n = 84

added 20% dropout **n = 105patients**

Largest sample size was obtained from calculation is total (n= 110).

Final sample size = 110 patients

15.0 Sampling method, subject recruitment and withdrawal criteria.

All participant who fulfills the inclusion criteria are enrolled after parental consent. All eligible participants within the 15 months recruitment will be included.

All participants will be given a 3-monthly follow-up at the paediatric endocrine clinic and at least 2 times will be seen during the study period. Each participant will be given 'weight diary" in which the monthly weight increment, dietary counseling and lifestyle education available in this diary. The participant needs to do monthly weight measurement at the nearest health clinic. The serial weight measurements will be written on weight diary. The researcher will make a phone call monthly to remind the participant for the weight measurement and they only allow to postpone the measurement within one week from the expected time.

The data on age, gender, dietary pattern, sedentary lifestyle and socioeconomic status of the family were collected using questionnaire. 24 Hour dietary recall will be interviewed by endocrine team doctor and the calorie intake will be calculated using Atlas of Food Exchanges and Portion Size UKM. The dietary pattern will be concluded as carbohydrate-fat rich diet or not.

Height and weight are measured by trained person. Weight is measured while the subjects were dress minimally without shoes in upright position using same standing stadiometer and recorded to the nearest 0.1kg. Height is measured to the nearest 0.5 cm in a standing position, without shoes on a standard height board. Blood pressure was measured with the digital method using appropriate cuff and standard sphygmomanometer that calibrated regularly.

Waist circumference is measured over the skin midway between the tenth rib and the iliac crest at the end of normal expiration, using same measuring tape. Body mass index

(BMI) is calculated using the formula: weight (kg)/height $(m)^2$. Anthropometric measurement will be done each follow up as a routine examination at pediatric endocrine clinic. The obesity is defined as BMI >95th centile of standard WHO BMI. Pubertal maturation is evaluated according to standardszed Tanner staging. All the physical examination and the pubertal maturation will be done by the endocrine team doctor at the endocrine paediatric clinic as a part of the service.

For biochemical measurements, a total of 10 ml venous blood sample will be obtained in the morning using standard venepuncture after overnight fast by trained health staff. Fasting lipid profiles: triglycerides, total cholesterol, high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL), fasting blood glucose, and insulin level. Thyroid function test, liver function test and renal functions test are also assessed. Oral glucose tolerance test (OGTT) will be performed for all patients as they are at risk of diabetes. All the blood parameter taken is a part of standard and routine investigation at the pediatric endocrine clinic and no extra blood needed for the research purpose. The index for insulin resistance is calculated using the homeostasis model assessment (HOMA) calculator version 2.2 taking scores > 3.16 as the existence of insulin resistance.[6] HOMA will be done twice for each participant in which first during the first contact and second is 6 months later. The HOMA index will be calculated using the investigation result from the routine blood taking and no extra blood need for it. The researcher will trace the investigation result from the folder only.

16.0 Statistical Analysis

SPSS IBM version 24.0 will be used to analyse the data. Median time to gain 1, 3 and 5 kg weight will be determine using Kaplan-Meier survival analysis. Factors which influencing time for weight gain will be determined using both simple and multiple cox-

regression analysis. For all statistical analysis, level of significant was set at 0.05. Correlation between this rate of weight gain and HOMA-IR will be analyse using Pearson's or spearman's correlation analysis.

17.0 Research tool

All the data are collected using questionnaire. Weight Diary will be used to monitor monthly weight and the participant need to do weight measurement at the nearest health clinic. The researcher will call the participant to remind them for monthly weight measurement. All the weight measurement needs to be written down on the weight diary and will be reviewed during follow up at paediatric endocrine clinic.

The 24-Hour Dietary Recall will be used to determine the dietary pattern of the participants. The interviewed session will be conducted by endocrine team doctor at the paediatric endocrine clinic and the calorie will be calculated using Atlas of Food Exchanges and Portion Size UKM.

OBESITY DATABASE

1. IDENTIFICATION

Date :

Study number :

DOB :

Race :

Birth weight :

Age at onset of obesity :

2. DEMOGRAPHIC DATA

1. Age :

2. Gender :

3. Socioeconomic of family

Income : RM----------

Education

- ☐ Tertiary education
- ☐ Secondary school
- ☐ Primary school
- ☐ No qualification

4. Lifestyle Behavioural

1. How long do you spend your time in a day for moderate exercise?

(Berapa lama anda menghabiskan masa anda sehari untuk bersenam sederhana?)

(eg: slow bike riding, brisk walking, walking to and from school, playing sport at lunch time or after school, doing an exercise class, doing housework)

(contoh : menunggang basikal perlahanan, berjalan pantas, berjalan pergi atau balik ke sdekolah, bermain sukan semasa waktu tengahari atau selepas balik sekolah, melakukan kelas latihan, melakukan kerja rumah)

☐ None ☐ < 15 min ☐ 15-30min ☐ > 30min-60min ☐ >60 min

2. How long do you spend your time a day for watching TV, playing video games, using computer/tablets/handphone for entertainment?

(Berapa lama anda menghabiskan masa dalam sehari untuk menonton televisyen, bermain permainan video atau mengunnakan komputer, komputer riba atau telifon untuk hiburan?)

☐ None ☐ < 1hr ☐ 1hr-2hr ☐ >2hr

1. **Dietary Intake (Using 24 H Dietary Recall)**
   Dietary data will be summarized for eg carbos: how many percent of a total.

   (the interview session will be conducted by endocrine team doctor)

EXAMINATION

Weight :…….

Height :…….....

BMI :……...

Waist Circumference :……..

Blood pressure :.....

Tanner Staging : .....

LABARATORY

FBS :…….....

FASTING INSULIN :……

MOGTT :.....(pre).....(post)

HOMA-IR CALCULATION:.....

LIPID PROFILE: HDL…… LDL:…….. VLDL:…….

TG:……..MMOL/L TOTAL CHOLESTEROL:……..MMOL/L

TFT :T4 : ..... TSH:……..

LFT :T.PROTEIN:……. AST:……..... ALT:……..ALP :.....

RFT: urea:.....creatinine :……

18.0 Dummy table

Table 1:

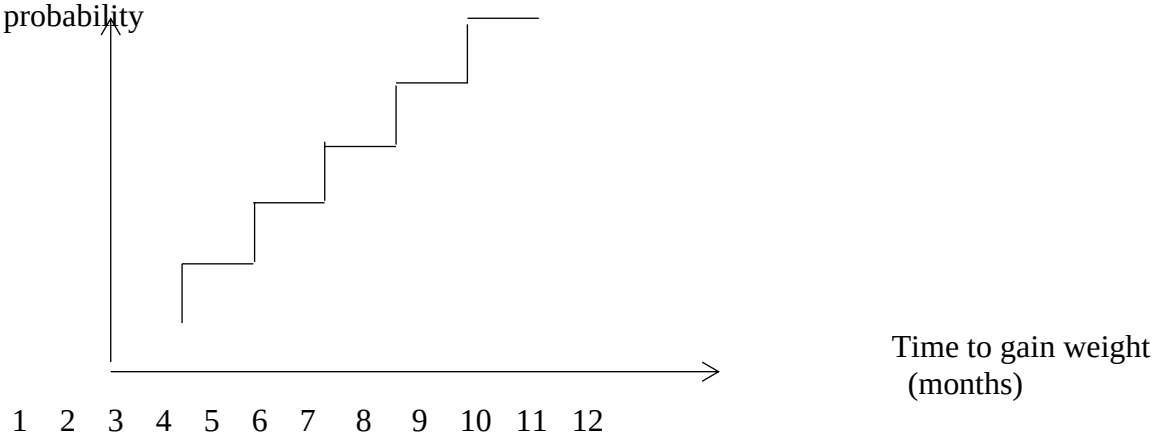


Table 2 : Demographic details for overall subject (n =110)

Variables	n(%)
Age	
Age group *	
2-9	
10-18	
Gender	
Male	
Female	
Eating habit	
Non carbohydrate- fat rich diet	
Carbohydrate-fat rich diet	
Life style	
Non sedentary	
Sedentary	
Socioeconomic status	
Income	
Low income	
Non low income	
Education	
Tertiary education	
Secondary school	
Primary school	
No qualification	

Footnote: * mean (SD)

Tablet 3: Simple Cox Regression (n=110)

Variable	Crude b	Crude HR (95%CI)	Wald statistic	p-value
Age				
Age group				
2-9				
10-18				
Gender				
Male				
Female				
Eating habit				
Non carbohydrate- fat rich diet				
Carbohydrate-fat rich diet				
Life style				
Non sedentary				
Sedentary				
Socioeconomic status				
Income				
Low income				
Non low income				
Education				
Tertiary education				
Secondary school				
Primary school				
No qualification				

Tablet 3: Multiple Cox Regression (n=110)

Variables	Adj b	Adj HR (95% CI)	Wald statistics	p-value
Age				
Age group				
2-9				
10-18				
Gender				
Male				
Female				
Eating habit				
Non carbohydrate- fat rich diet				

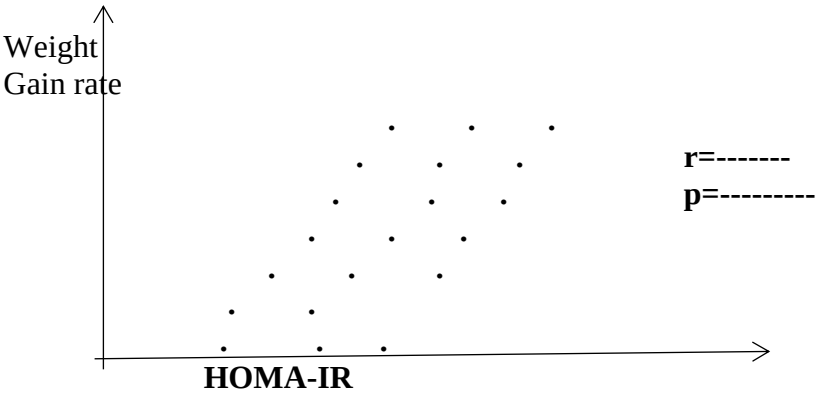
Carbohydrate-fat rich diet

Life style
Non sedentary
Sedentary

Socioeconomic status
Income
Low income
Non low income

Education
Tertiary education
Secondary school
Primary school
No qualification

Table 4 : Correlation between rapid weight gain and HOMA-IR.



20.0 Gant chart

Activities	Sep2018 – January 2019	Jun 2019-September 2020	October 2020-Dec 2020	Jan 2021-Mac 2021
Research activities proposal				
Recruitments				
Data analysis/interpretation				
Thesis write up				

1.0 Ethical consideration.

1. Subject vulnerability

The participants are all obese subjects referred to us, under parental autonomy and decision-making. Complete parental consent is used.

2. Declaration of absence of conflict of interest

There is a conflict of interest as we are hoping to see more patients with rapid weight gain to see its correlation with HOMA-IR. However, patient's right is not compromised since we still provide the treatment and intervention of the obesity as nonparticipant children. Therefore, we might have difficulty to achieve the calculated sample size.

3. Privacy and confidentiality

Confidentiality of the data will be maintained at highest level as possible which only researcher will have the access to the data. All forms are anonymous and will be entered into SPSS software. Only research team members can access the data. Data will be presented as grouped data and will not identify the responders individually.

4. Community sensitivities and benefits

No part of this study may trigger social stigma. This study will benefit the community in term of identify the factors that influence the time to gain weight and whether the rapid increment of weight can contribute to insulin resistance or not. Therefore, the early detection can provide early prevention strategies.

22.0 Principal investigator and Co investigator qualification.

Dr Siti Hasmiza Binti Che Mat completed his Medical Degree from University Teknologi Mara (UiTM). Currently second year master student in medicine (paediatric).

Dr Suhaimi Bin Hussain graduated from USM and currently he is a consultant Paediatric Endocrinologist in Paediatric Department Pusat Pengajian Sains Perubatan University Sains Malaysia.

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