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ORIGINAL ARTICLE

Prevalence of dysglycemia and its associations with age and body mass index among community dwelling adults in a developing country

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Abstract

Introduction Dysglycemia includes prediabetes and diabetes. We aimed to study the prevalence of dysglycemia, and its associations with age and body mass index (BMI) among community dwelling adults in Sri Lanka.

Methods The prevalence of dysglycemic state (FPG > 100 mg/dL) and its associations with age and BMI in males and females were estimated. The association between gender and glycemic status in different BMI ranges and age groups were estimated. The optimal cut-off points of BMI to determine the risk of dysglycemia in both genders were calculated.

Results Prevalence of prediabetes and diabetes of females were 25.3% and 16.4% and of males were 26.2% and 17.4% respectively. Dysglycemia showed a significant positive correlation with age in both genders and a significant positive correlation with BMI in males ($p < 0.05$). Aging (OR = 1.05, CI 1.02–1.08, $p < 0.001$) and increasing BMI (OR = 1.10, CI 1.05–1.15, $p < 0.001$) of males and aging (OR = 1.04, CI 1.02–1.06, $p < 0.001$) of females are significantly associated with dysglycemia. The optimal cut-off point of BMI for males was 22.86 kg/m^2 (sensitivity 76.6%, specificity 53.9%) to determine the risk of dysglycemia.

Conclusions Four out of ten adults in the screened population were dysglycemic. An increase in BMI is significantly associated with dysglycemic status in males compared to females. The recommended cut-off value of BMI as 23 kg/m^2 for South Asian population to categorize overweight individuals has an adequate sensitivity to recognize dysglycemic adult males but not the females in this community.

Keywords Dysglycemia · Body mass index · Fasting plasma glucose · Obesity · Prevalence

Introduction

Dysglycemia in the form of either pre-diabetes or diabetes mellitus (DM) is a leading metabolic abnormality which affects individuals in the developing as well as in developed countries [1]. The early stage of dysglycemia is termed as pre-diabetes and includes individuals with impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG). The global prevalence of pre-diabetes is rising rapidly and is estimated that number of people with pre-diabetes in the age group of 20–79 years is 352 million in 2017. The numbers are predicted to reach 587 million by the year 2045 [2]. A substantial majority of these people live in low- and middle-income countries. According to the International Diabetes Federation (IDF) data, the prevalence of IGT is 3.0% in people aged 20–79 years in the South East Asia region [2]. People with pre-diabetes have a high risk of developing DM and its associated comorbidities especially cardiovascular diseases [2]. The prevalence of DM is increasing globally and the IDF has estimated as 415 million adults suffer from DM at present and this number will reach to 642 million by 2040 [3]. Notably, the number of individuals living in the South East Asian region with DM has risen sharply during the past few years. The IDF has estimated that 6.8–10.8% of the adult population is living with DM in the South East Asian countries [3]. Environmental changes, behavioral

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patterns, and lifestyle changes of people resulted in escalating rates of development of DM in this region [4, 5].

According to the recent estimates of IDF, prevalence of diabetes among adults in Sri Lanka is 8.6% [2]. Subsequent problems due to high prevalence of DM have become a major health care burden in Sri Lanka. Therefore, screening of individuals for dysglycemia which includes both categories of prediabetes and diabetes seems important and cost effective practice to prevent or delay the occurrence of hyperglycemia associated complications. The commonly available tools for screening dysglycemic state are fasting plasma glucose (FPG) concentration, oral glucose tolerance test (OGTT) and percentage of glycated hemoglobin (HbA_{1C}). The American Diabetes Association (ADA) has defined the individuals who have pre-diabetes as IFG measured by FPG level 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L), or IGT measured by 2-h values in the OGTT test of 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) [6]. Even though pre-diabetes status is defined using HbA_{1C} as 6.0 to 6.5% range, it fails to identify a considerable number of patients who have IFG and/or IGT. Individuals with FPG concentration $\geq$ 126 mg/dL ($\geq$ 6.9 mmol/L), OGTT $\geq$ 200 mg/dL ($\geq$ 11.0 mmol/L), and HbA_{1C} level $\geq$ 6.5% are classified as patients with DM [6]. According to the recent findings, HbA_{1C} cutoff values for diabetes vary across different ethnicities and geographical regions compared to FPG and OGTT cutoff values. Studies carried out in different settings have proposed several cutoff values for HbA_{1C} [7, 8] and for Sri Lankans, it was reported as $\geq$ 6.3% according to a local study [9].

Epidemiological studies have revealed that increasing age and body mass index (BMI), prevalence of dyslipidemia, hypertension, and family history of DM are important and well-established risk factors associated with dysglycemia. Among these factors, increasing age and BMI were considered in the present study. A recent study has found several associations between increasing BMI and dysglycemia operating via proinflammatory cytokines (tumor necrosis factor and interleukin-6), insulin resistance, deranged fatty acid metabolism, and cellular processes such as mitochondrial dysfunction and endoplasmic reticulum stress [10]. The BMI, calculated as weight (kg) divided by height square (m^2), is the most common method of assessing overweight and obesity in routine clinical practice. The World Health Organization (WHO) has defined the cut-off points of BMI to classify overweight and obesity as 25 kg/m^2 and 30 kg/m^2 respectively based on the epidemiological evidence investigating associations with mortality and morbidity [11]. The evidences on these cut-off points originate from white populations, and the level of risk associated with the classification of overweight and obesity vary across racial groups. Based on this, an expert committee of the WHO has recommended revised cut-off points to classify overweight and obesity as 23 kg/m^2 and 27.5 kg/m^2 respectively for the Asian population [12]. However, further evidences suggest that these revised cut-off points exert some limitations at the determination of risk of some epidemic diseases in Asians [13, 14].

Previous studies revealed the association of dysglycemia and its associated comorbidities and mortality with increasing age [15, 16]. Factors such as increasing insulin resistance and impaired pancreatic islet cell function are linked to the increased prevalence of dysglycemia with aging [17]. The age-related increase in insulin resistance is associated with adiposity, sarcopenia, and physical inactivity which has also been identified as risk factors for dysglycemia [18]. Furthermore, vitamin D deficiency is one of the factors accelerating insulin resistance, obesity and DM [19–21]. The ADA recommends to screen individuals having high BMI with other risk factors and all others aged $\geq$ 45 years for dysglycemia at a minimum of three-year intervals using one of the screening tools such as FPG, OGTT, or HbA_{1C} [17].

Even though the associations of risk factors with dysglycemia and the gender differences are well established, whether the association of dysglycemia with increasing age and BMI is similar in both genders has not been explored previously in the Sri Lankan population. Based on all these, we aimed to study the gender wise prevalence of glycemic status, its associations with age and BMI and to determine an optimal cutoff of BMI to assess the risk of dysglycemia in the Sri Lankan population.

Materials and methods

Study design

This study was a community based cross-sectional study conducted in randomly selected divisional secretariat areas of semi urban localities in Southern Sri Lankan city of Galle, during February 2018 to September 2019. A cluster sampling method was used to recruit study subjects. Prior to the commencement of the study, the study was clearly explained to the study population by the researchers.

Study population and study sample

The present study was the first phase of a clinical trial designed to test the efficacy of a herbal drug in newly diagnosed individuals with type 2 diabetes mellitus. To assess the prevalence of newly diagnosed type 2 diabetes mellitus, considering a confidence limit of 95%, expected

prevalence of newly diagnosed type 2 diabetes mellitus as 10% and a precision of 0.05, the required sample size was 138. Five divisional secretariat areas were randomly selected to enroll the participants. With an estimated design effect of 1.5 for cluster sampling, 207 individuals from each selected divisional secretariat area were required. Assuming that the prevalence of type 2 diabetes mellitus in each of those selected areas was different, the minimum sample required for the study was 1035. Considering 20% of non-responders and screen failures, a minimum of 1250 subjects were required. In the present study, a total number of 1691 individuals were invited to participate.

Five divisional secretariat areas were randomly selected from the total of 19 divisions following the simple random sampling method using excel based random number generation. A number of seven "Grama Niladhari" divisions (divisions similar to wards or villages) were selected randomly from each of the selected divisional secretariat areas following the simple random sampling method. An average number of 48 individuals (belong to age group of 30–60 years) were recruited for the present study from each of selected "Grama Niladhari" division. One eligible individual was selected randomly from one household. A random starting point was identified and the households on either side of the road in a randomly determined direction were visited to identify and select eligible individuals until the required numbers from each "Grama Niladhari" division were being enrolled. Patients with previously diagnosed diabetes both type 1 and type 2, and who were on long term steroids for chronic disorders and pregnant women were excluded from the study.

Detection of indices

Demographic and anthropometric parameters such as age, gender, height and weight were collected from all participants. Weight was measured using a portable scale without shoes and height was measured using a height bar in standing position without shoes while keeping the shoulder in erect position. Subjects with a BMI below 18.5 kg/m^2 were classified as underweight, between 18.5 and 22.9 kg/m^2 as normal, between 23.0 and 24.9 kg/m^2 as overweight, and equal or larger than 25.0 kg/m^2 were classified as obese.

Overnight fasting (8–10 h) venous blood samples were collected from each participant. Collected blood samples were stored in an ice bath till the delivery to laboratory. The separated plasma samples were stored at − 80° C until analyzed. FPG concentration was estimated by glucose oxidase method. Dysglycemia was diagnosed based on the ADA recommended criteria [6]. FPG concentration < 5.6 mmol/L and ≥ 5.6 mmol/L were considered normoglycemia and dysglycemia respectively [6]. FPG concentration between 5.6 mmol/L to 6.9 mmol/L and ≥ 6.9 mmol/L were considered pre-diabetes and diabetes respectively.

Statistical analysis

Data were analyzed using the version 25.0 of Statistical Package for Social Sciences (SPSS) software. The continuous variables were presented as mean ± SD while the categorical data were expressed as percentages. Normality of the data sets was checked using Kolmogorov–Smirnov test. Descriptive data of both genders were compared using independent sample t-test. The correlation between FPG values and anthropometric measures of age and BMI were assessed in both genders through the linear correlation analysis. Binary logistic regression was used to calculate odds ratio for the association of age and BMI (independent variables) with dysglycemia as the dependent variable in both genders. The chi-square test was used to assess the association between gender and glycemic status in each of BMI categories and age groups. Receiver operating characteristic (ROC) curves were developed for BMI values of both genders separately as a risk factor of dysglycemia. The optimal cut-off point of BMI was determined using Youden index (maximum [sensitivity + specificity − 1]) [22]. $p \leq 0.05$ was considered statistically significant.

Results

Although 1691 individuals were invited for the screening programs, only 1334 individuals participated with a non-response rate of 21.1%. The eligible population consisted of 1120 individuals with 803 (71.7%) females and 317 (28.3%) males. Figure 1 shows the flow diagram of the recruitment of eligible participants for the present study.

Mean age, BMI and FPG concentration of female subjects were 45.7 ± 9 years, 26.8 ± 6.4 kg/m^2 and 5.9 ± 2.1 mmol/L respectively. Mean age, BMI, and FPG concentration of male subjects were 44.5 ± 8.1 years, 24.8 ± 5.5 kg/m^2, and 6.0 ± 2.2 mmol/L respectively (Table 1).

Of the total number of females, 468 (58.3%) were normoglycemic, 203 (25.3%) were pre-diabetic, and 132 (16.4%) were detected to have diabetes. Among the male population, 179 (56.5%) individuals were normoglycemic, 83 (26.2%) were pre-diabetic, and 55 (17.4%) were detected to have diabetes. The gender wise prevalence of glycemic status diagnosed by FPG concentration is summarized in Table 2.

Glycemic status diagnosed by FPG concentration showed a significant positive correlation with the age in both genders and a significant positive correlation with BMI in males (Table 3).

Regression analysis revealed that increase in age and BMI in the whole population are significantly associated with

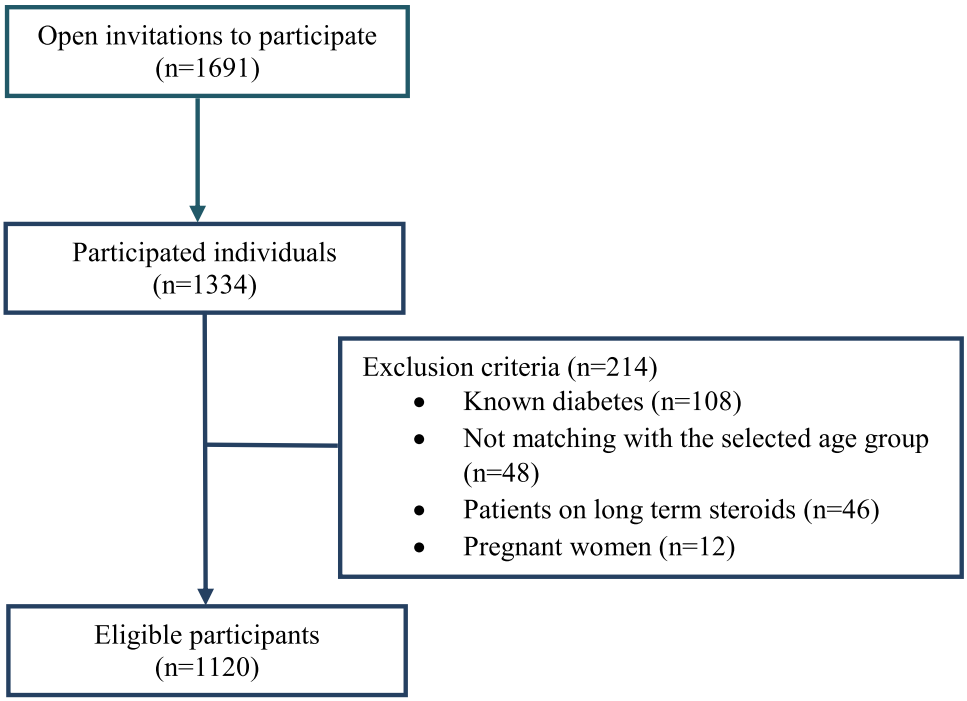

Fig. 1 Flow diagram for the recruitment of eligible participants

Table 1 Descriptive statistics of the participants

	Female		Male		*p* value
	Mean	SD	Mean	SD	
Height (cm)	149.4	10.9	161.6	11.0	0.000
Weight (kg)	57.0	10.6	64.2	12.1	0.000
BMI (kg/m^2)	26.8	6.4	24.8	5.5	0.095
Age (years)	45.7	8.7	44.6	7.9	0.037
FPG (mmol/L)	5.9	2.1	6.0	2.2	0.450

BMI, body mass index; *FPG*, fasting plasma glucose

Table 2 Prevalence of glycemic status according to gender

Glycemic status	Number of females	%	Number of males	%
Normoglycemia	468	58.3	179	56.5
Pre diabetes	203	25.3	83	26.2
Diabetes	132	16.4	55	17.4

dysglycemia (Table 4). When considering the gender wise associations, increase in age in both genders and increase in BMI only in males were significantly associated with dysglycemia (Table 4).

As shown below, the prevalence of normoglycemia decreased and the prevalence of dysglycemia increased with rising BMI and age in both genders (Figs. 2 and 3).

Results of the chi-square test showed that there is a significant difference between gender and glycemic status in normal weight (X^2 (1) = 7.663, $p = 0.006$) and obese (X^2 (1) = 7.476, $p = 0.006$) categories. However, there is no association between gender and glycemic status diagnosed by FPG concentration in any of the considered age groups.

Figure 4 shows the ROC curve of BMI to assess the risk of dysglycemia for both genders separately. The area under the ROC curve (AUC) of females was not-significant (0.516 ± 0.021, $p = 0.43$) whereas ROC curve for males was significant (0.651 ± 0.031, $p = 0.000$) in assessing the risk of dysglycemia by means of BMI. The optimal cut-off value of BMI for males was 22.86 kg/m^2 (sensitivity 76.6%, specificity 53.9%) to determine the risk of dysglycemia.

Table 3 Gender wise correlations between glycemic status vs age and BMI

	Females		Males	
	Age	BMI	Age	BMI
FPG	$r = 0.158$ $p = 0.000$	$r = 0.003$ $p = 0.932$	$r = 0.160$ $p = 0.004$	$r = 0.162$ $p = 0.004$

BMI, body mass index; *FPG*, fasting plasma glucose

Table 4 Study population associations of age and BMI with dysglycemia

	Variable	OR	95% CI	*p* value
Whole population	Age	1.04	1.03–1.06	0.000
	BMI	1.03	1.01–1.05	0.006
Females	Age	1.04	1.02–1.06	0.000
	BMI	1.01	0.99–1.03	0.474
Males	Age	1.05	1.02–1.08	0.000
	BMI	1.10	1.05–1.15	0.000

BMI, body mass index

Discussion

Results of the present study revealed high prevalence of dysglycemia in the community and the gender specific associations of two major risk factors namely increasing age and BMI. The cutoff value of FPG ≥ 5.6 mmol/L (100 mg/ dL) was used to define dysglycemia as the value is well established universally with considerable specificity and sensitivity. One of the important findings of the present study is almost four out of ten adults suffer from dysglycemia either in the form of pre-diabetes or diabetes. Further, the prevalence of pre-diabetes (26.2%) as well as diabetes (17.4%) is higher in males than that of females as 25.3% and 16.4% respectively. Although there are no previously reported facts on the prevalence of dysglycemia, a higher prevalence of diabetes in men (14.2%) than in women (13.5%) in four provinces in Sri Lanka by involving of individuals between 35 and 65 years of age has been reported [23]. Similar observations were made in the studies carried out in different settings [24, 25] and is suggested that high prevalence of DM in males than in females is due to gender specific differences in visceral fat accumulation [24]. However, the exact mechanism related to the higher prevalence of dysglycemia in males than in females is still unclear and further investigations are warranted. Our study is the most recent population-based study conducted with an aim of estimating of the prevalence of dysglycemia. With respect to the preexisted prevalence of diabetes mellitus in Sri Lanka [23], the present study clearly indicated a dramatic increment in newly diagnosed cases of diabetes mellitus in Galle, as one of the rapidly growing cities in Sri Lanka. The spatial structure of Galle is being subjected to changes over the time by expanding the growth towards outer city. This scenario has made significant changes in the city structure as well as in the lives of resident individuals and as a result

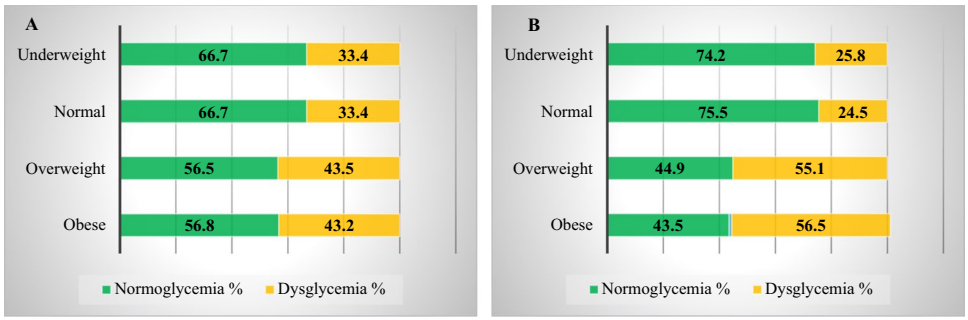

Fig. 2 Prevalence of glycemic status according to BMI in **A** females **B** males

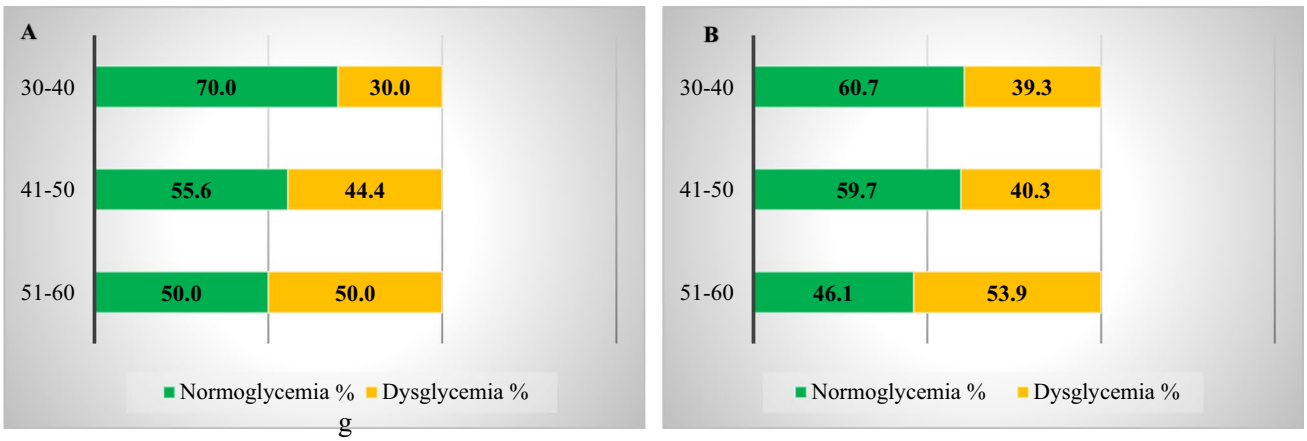

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Fig. 3 Prevalence of glycemic status according to age in **A** females **B** males

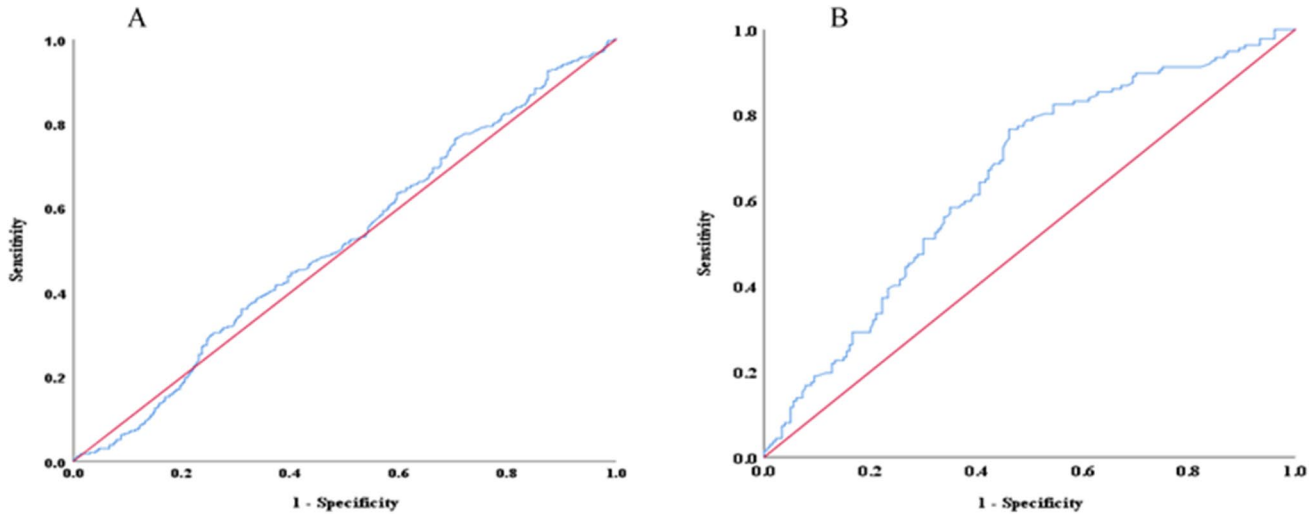

Fig. 4 ROC curve for BMI as the risk of dysglycemia in **A** females **B** males

the individuals are on unhealthy diet, physical inactivity etc. All these facts might contribute for this increment of high prevalence of newly detected cases of dysglycemia and further studies are warranted on this concern. In contrast, a high prevalence of dysglycemia was seen in females than in males in a study conducted in rural, urban and plantation sector in Kalutara district, Western province, Sri Lanka by involving 1300 adults between aged of 35 to 64 years [22].

Findings of the present study also revealed that FPG concentration was significantly and positively correlated with age in both genders whereas significant association with BMI was seen only in males. Furthermore, the binary logistic regression analysis revealed that increase in age of both genders and BMI of males are significantly associated with dysglycemia. Although the development of dysglycemia is multifactorial, insulin resistance and decrement of the pancreatic insulin secretion are well reported pathogenetic mechanisms associated with dysglycemia. Age is the one of the most important factors which affects these mechanisms. Development of insulin resistance with increasing age of population has also been demonstrated using hyperinsulinemic-euglycemic clamp method [26] and responsible factors for the reduced insulin effectiveness with aging have been summarized as increased abdominal fat mass, decreased physical activity, mitochondrial dysfunction, hormonal changes, increased oxidative stress and inflammation [27]. Indeed, the prevalence of dysglycemia has increased rapidly with aging in the past decades and management of dysglycemia in elders is very complicated as they commonly have several co-existing health issues that could affect the overall management of patients.

Over the past decades, progressive increase in body weight among individuals in developed countries than in the low- or middle-income developing countries has been reported [28]. A recent trend of similar weight gain among individuals is highlighted in developing countries as well [29]. The mean BMI values of females (26.8 ± 6.4 kg/m^2) and males (24.8 ± 5.5 kg/m^2) found in our study were in the range of obese and overweight respectively. These values suggest a possible interplay of genetic factors, westernized lifestyle, physical inactivity etc. among Sri Lankans as a nation living in a developing country of South East Asian region. According to the classification of BMI, our results revealed that the prevalence of dysglycemia is increased with an increment in BMI in both genders. Moreover, the present study disclosed that there is a significant difference between the gender and glycemic status in normal weight and obese categories. The male population with normal weight has the lowest prevalence of dysglycemia (24.5%). However, in the obese category, males have the highest prevalence of dysglycemia (56.5%). This might be due to their careless behavior in the management of early stage of dysglycemia because of their occupational activities and their habits including smoking and addiction to intake of alcohol. In fact, males are often the breadwinners of the family and hence more likely to be employed than females in the South East Asian countries including Sri Lanka. These factors also influence the inclusion of a smaller number of males than females in the community screening programs as in the present study. However, further research is warranted to rectify this finding.

As it was important to determine the optimal cut-off points of BMI to assess the risk for dysglycemia, ROC curves were drawn for both genders separately. According to the results, cut-off value for BMI in males was 22.86 kg/m^2 with 76.6% sensitivity and 53.9% specificity. The AUC value for BMI (0.651) in ROC analysis unveiled that

BMI > 22.86 kg/m^2 could be used as an acceptable clinical parameter to determine the risk of dysglycemia among adult males in this community. The observed BMI cut-off point of 22.86 kg/m^2 is very close to the WHO recommended revised cut-off value for overweight (23 kg/m^2) among the South Asian population. However, since the AUC value of BMI for females is almost 0.5 (0.51), this was not further subjected to estimate sensitivity or specificity.

The main strength of this study was its community-based design to detect previously undetected dysglycemia and the study of gender wise differences in association of age and BMI with dysglycemia in a developing South East Asian country during an era of an obesity pandemic. Our findings highlight the rising burden of both dysglycemia and obesity among adults in a developing country in this region. It also strengthens the use of recommended cut-off value of 23 kg/m^2 for the South Asian region to categorize overweight individuals especially the males in this population. However, even with higher representation of females (72%) in the study sample, similar conclusion for females could not be arrived from our findings. We hope the findings would stimulate further studies to determine the possibility of distinct gender-based association of obesity and dysglycemia in this community. Without analyzing the results of such large-scale studies, it would be premature to predict the necessity to adopt separate, gender specific BMI cut-off values to categorize overweight and obesity as in the case of using separate cut-off values of waist circumference for defining central obesity for males and females. Conducting the study in a limited geographical locality in Southern Sri Lanka, the presence of relatively high female representation in the study sample and the use of FPG test results instead of the gold standard OGTT to screen dysglycemia are the main limitations of this study.

Conclusions

The prevalence of dysglycemia either in the form of prediabetes or diabetes in the male population (43.6%) is higher than that of the female population (41.7%) in this cohort. An increase in age in both genders and BMI in males is significantly associated with dysglycemia. The cut-off value of BMI > 22.86 kg/m^2 could be used as an acceptable clinical parameter to determine the risk of dysglycemia by means of overweight among the male population in Sri Lanka. Hence, the WHO recommended cut-off point of 23 kg/m^2 is further corroborated for the male population in Sri Lanka in assessing the risk of dysglycemia by means of overweight. Based on the finding of this study, it is important to implement measures to control overweight and obesity more vigorously in males to reduce the onset of dysglycemia.

Declarations

Ethical considerations Ethical clearance for the study was granted by the Ethical Review Committee, Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka (14.06.2017:3.9). Written informed consent was obtained from each one of the participants who underwent screening.

Conflict of interest Authors have declared that they have no conflicts of interest.

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