Prevalence of different states of glucose intolerance in Sri Lankan children and adolescents with obesity and its relation to other comorbidities

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Abstract

Background: South Asian adults have higher prevalence of obesity comorbidities than other ethnic groups. Whether this also is true for Sri Lankan children with obesity has rarely been investigated.

Objective: To investigate prevalence of glucose intolerance and other comorbidities in Sri Lankan children with obesity and compare them with Swedish children. To identify risk factors associated with glucose intolerance.

Subjects: A total of 357 Sri Lankan children (185 boys), aged 7 to 17 years with BMI-SDS $\geq$ 2.0 from a cross-sectional school screening in Negombo. A total of 167 subjects from this study population were matched for sex, BMI-SDS and age with 167 Swedish subjects from the ULSCO cohort for comparison.

Methods: After a 12 hour overnight fast, blood samples were collected and oral glucose tolerance test was performed. Body fat mass was assessed by bioelectrical impedance assay. Data regarding medical history and socioeconomic status were obtained from questionnaires.

Results: Based on levels of fasting glucose (FG) and 2 hours-glucose (2 hours-G), Sri Lankan subjects were divided into five groups: normal glucose tolerance (77.5%, $n = 276$), isolated impaired fasting glucose according to ADA criteria (9.0%, $n = 32$), isolated impaired glucose tolerance (8.4%, $n = 30$), combined impaired fasting glucose (IFG) + impaired glucose tolerance (IGT) (3.1%, $n = 11$) and type 2 diabetes mellitus (2.0%, $n = 7$). FG, 2 hours-insulin and educational status of the father independently increased the Odds ratio to have elevated 2 hours-G. Sri Lankan subjects had higher percentage of body fat, but less abdominal fat than Swedish subjects.
INTRODUCTION

Rising childhood obesity rates worldwide lead to an increase in the prevalence of obesity-related complications, such as type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), hypertension and other non-communicable diseases, and to a decrease in the age of onset. The World Obesity Federation estimated in a report, using data from the Global Burden of Disease collaborative, that by 2025 globally some 268 million children aged 5 to 17 years may be overweight, including 91 million with obesity. They also estimated the likely numbers of children in 2025 with obesity-related comorbidities like impaired glucose tolerance (IGT, 12 million) and T2DM (4 million).1

Disturbances of glucose metabolism, such as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), are common among children and adolescents with obesity all over the world. High prevalence rates of IGT in children and adolescents with obesity between 15% and 25% have been reported from the United States,2 Bangladesh,3,4 Thailand5 and Iran.6 Prevalence rates of IGT in Europe are generally lower with rates between 3% and 5%, for example, in Italy7-10 and the Netherlands,11 but reported prevalence varies significantly with higher rates of 15% to 19% observed in some studies from Spain12 and Montenegro,13 and 11% reported from Austria.14 Some Scandinavian studies also observed high prevalence of both IGT14 and especially IFG, which seems to be more common in northern European countries than in other parts of Europe.15,16 There are only sparse data regarding the prevalence of glucose intolerance in South Asian and especially in Sri Lankan children with obesity, but one recent study in 202 children with obesity from Colombo reported a prevalence of 11.4% for IGT and 10.9% for IFG (according to ADA criteria).17

Among Sri Lankan adults, the prevalence of T2DM was about 10.3% in a study conducted from 2005 to 2006, and some form of dysglycemia was present in 21.8% of the participants.18 The same study claimed a projected diabetes prevalence of 13.9% in Sri Lanka for the year 2030. Compared with many other ethnic groups, South Asian populations are, due to their fast economic growth and genetic predisposition, prone to develop many adverse metabolic consequences at an earlier degree of obesity, including insulin resistance,19 glucose intolerance, and T2DM.20 A WHO expert consultation concluded that the proportion of Asian people with a high risk of developing T2DM and cardiovascular disease is substantial at BMI values lower than the existing WHO cut-off point for overweight (> 25 kg/m²).21 Furthermore, people born in the Indian sub-continent who had migrated to England and Wales were found to have higher morality from both ischemic heart disease and cerebrovascular disease than the national average.22 Another study compared the relationship between obesity and prevalent diabetes across ethnic groups in the UK Biobank cohort and found that for the equivalent prevalence of diabetes at 30 kg/m² in white participants, BMI equated to 22.0 kg/m² in South Asians.23

The overall observation is that South Asian adults have higher prevalence of comorbidities at the same BMI compared with other ethnic groups. Whether this also is true for Sri Lankan children with obesity particularly compared to obese children of other origins has rarely been investigated. One previous study examined whether British South Asian children differ in insulin resistance, adiposity, and cardiovascular risk profile from white children, and found that the tendency to develop insulin resistance observed in British South Asian adults was also apparent in children.24 Another study in 6 to 11 year old randomly selected South Indian children with different weight status showed an overall prevalence of prediabetes or diabetes of 3.7%, with the highest prevalence of 12.7% in girls with abdominal obesity.25 A recent study in 5 to 15 year old randomly selected Sri Lankan children from the Colombo district found that insulin resistance among Sri Lankan children was high in all groups of weight status, even if many children were able to control glucose levels within normal limits.26 Even if these studies suggest a relatively high prevalence of glucose intolerance in South Indian and Sri Lankan children with obesity, the data has not been compared with data from children with obesity of other ethnic origins.

The aim of the present study was to investigate the prevalence of different states of glucose intolerance in Sri Lankan children and adolescents with obesity and its relation to other metabolic and anthropometric parameters. Furthermore, this study compared body composition and prevalence of obesity comorbidities among Sri Lankan and Swedish children with the same degree of obesity expressed as BMI-SDS.

METHODS

2.1 Study design and setting

All children identified as having obesity (BMI-SDS ≥ +2SD according to WHO, 2007) in a cross-sectional survey carried out in Sri Lankan schools27 were invited to the Diabetes Screening and Vocational Training Centre of the Lions Club of Negombo Host for further examination and possible treatment. Children with chronic diseases, secondary causes for obesity or on long term medication were excluded according to judgment of the clinical examiner. The original school screening was conducted between July 2013 and March 2014 in eight
schools in the Negombo educational zone of the Western Province of Sri Lanka. The assessments of children with obesity at the Diabetes Screening and Vocational Training Centre of the Lions Club of Negombo Host were carried out between July and September 2014.

2.2 | Study population

Out of 13,688 children participating in the school screening, 667 were identified as having obesity at screening, and the 500 that were 7 years or older were invited to the Diabetes Screening Centre. Of the 500 invited children with obesity, 430 came for assessments at the centre. Out of these 430 children, 404 completed baseline assessments, whereas 26 of them could not complete them due to difficulties to go through oral glucose tolerance test (OGTT). In the analysis, 357 children with complete OGTT and fulfilling the WHO criteria for obesity (BMI-SDS ≥ +2SD) were included (Figure 1).

2.3 | Baseline assessments

Baseline assessment at the Diabetes Screening and Vocational Training Centre of the Lions Club of Negombo Host was done after a 12 hour overnight fast. Height, weight,28 waist circumference (WC),29 and blood pressure were measured by trained research assistants using a standardized protocol. To limit the impact of inter-operator variability, the same six assistants who had undergone the same training conducted all the measurements. Height (cm) was assessed using a standardized, calibrated stadiometer and weight (kg) was assessed using a standardized, calibrated scale with the patient wearing light clothing and no shoes. WC (cm) was measured with a flexible tape midway between the superior border of the iliac crest and the lowest rib on the standing patient. BMI was calculated by weight (kg) divided by height squared (m²) and BMI-SDS was calculated using the software Microsoft Excel with the plugin LMSGrowth and the reference WHO 2007. The same software was used to calculate SDS for both systolic and diastolic blood pressure. Waist-height-ratio (WHtR) was calculated by dividing WC (cm)/height (cm). Pubertal staging was assessed using visual charts,30 and wherever subject and parents were not certain of the staging, with consent, the examiner assessed the correct pubertal stage. In boys, testis size was assessed by the examiner using Prader orchidometer.31

2.4 | Blood sampling

Blood was drawn, after applying lidocaine/prilocaine (Emla) anesthetic cream, to assess fasting glucose (FG), fasting insulin (FI), total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG), alanine transaminase (ALT), aspartate transaminase (AST), and highly sensitive C-reactive protein (hs-CRP). Serum was separated immediately and stored at −20°C and analysis was conducted in batches at the biochemical laboratory of the same centre.

2.5 | Oral glucose tolerance test

OGTT was performed after administering anhydrous glucose 1.75 g/kg body weight to a maximum of 75 g and blood was drawn 2 hours later for glucose (2 hours-G) and insulin (2 hours-I) measurements.

2.6 | Validation of glucose tolerance and metabolic derangements

IFG was defined by FG 100 to 125 mg/dL according to ADA (American Diabetes Association) criteria.32 IGT was defined by 2 hours-G between 140 and 199 mg/dL. T2DM was defined by 2 hours-G ≥ 200 mg/dL and/or FG ≥126 mg/dL. Based on levels of FG and 2 hours-G, the subjects were divided into five groups (representing states of glucose intolerance from NGT to T2DM) as having normal glucose tolerance (NGT), isolated impaired fasting glucose (iso-IFG), isolated impaired glucose tolerance (iso-IGT), combined IFG + IGT (comb IFG + IGT) or T2DM.

Other metabolic derangements were identified as: FI ≥12 μIU/mL33 TC ≥200 mg/dL (≥5.17 mmol/L), LDL ≥130 mg/dL (≥3.36 mmol/L), HDL <40 mg/dL (<1.03 mmol/L), TG ≥150 mg/dL (≥1.69 mmol/L),34 AST >40 IU/L, ALT >40 IU/L,35 hs-CRP >1 mg/dL.36 To assess insulin resistance, HOMA-IR was calculated as (FG×FI)/22.5 (FG in mmol/L,
Elevated blood pressure was defined as ≥ 2 SD for both systolic and diastolic blood pressure.  

2.7 | Body composition

Body fat mass (FM) was assessed by bioelectrical impedance assay (BIA) using a platform-type, eight electrode In-Body 230 instrument (InBody Biospace, South Korea), and % FM was expressed as a fraction of total body weight. The device has been validated against locally developed BIA prediction equations.

2.8 | Liver ultrasound

Ultrasound scan of the abdomen was conducted by an experienced radiologist using a Siemens Acuson X300, to detect and grade different stages of NAFLD. Results were reported as normal echogenicity or hepatic steatosis categorized from grade 1 to 3.

2.9 | Questionnaires

During assessments at the Diabetes Screening and Vocational Training Centre of the Lions Club of Negombo Host, the subjects and their parents were asked to complete a questionnaire about their medical history, socioeconomic status and family situation. One of the questions estimated the parents’ educational level using a scale from 1 (did not attend school) to 8 (post graduate training), where the options 1 to 4 were considered as lower educational level (“did not attend school” up to “grade 6 to 10”) and the options 5 to 8 as higher educational level (“O-level=more than 10 years of school” up to “post graduate training”). Data regarding medical family history, physical activity and nutritional habits were obtained from another questionnaire that was completed at the original school screening.

2.10 | Comparison with Swedish study population

For comparison of amount and distribution of body fat as well as metabolic and lifestyle parameters, data from Swedish children and adolescents with obesity included in the ULSCO (Uppsala longitudinal study of childhood obesity) cohort were used. The ULSCO cohort consists of children and adolescents who are referred from schools or other healthcare units to a pediatric specialist department for further treatment of obesity. Sri Lankan subjects were matched for sex and BMI-SDS (to the first decimal) as well as for approximate age (± 1 year) with Swedish subjects from the ULSCO cohort. The matching procedure resulted in a study population of 167 (95 boys) Sri Lankan and 167 (95 boys) Swedish subjects. Although 45% of the ULSCO subjects included for comparison had at least one parent born in another country than Sweden, only 1.75% (n = 7 subjects) had a parent with South Asian origin, none of them Sri Lankan. In the Sri Lankan study population, subjects of other than Sri Lankan origin, or who had not been living in Sri Lanka during the last 5 years, were excluded. Different ethnic groups within the Sri Lankan population (Singhalese, Tamils, Burghers/Eurasian, Moors/Muslims) were represented in the study population. Blood samples and anthropometric measurements from the Swedish subjects were collected according to the ULSCO protocol. For comparison of amount of body fat, body composition in the ULSCO subjects was calculated according to the manufacturer’s instructions using the bioimpedance devices InBody S20 (BioSpace, Seoul, Korea) or Tanita MC980 (Tanita Corporation, Japan) on a fasting subject who was instructed to empty the bladder before the examination. The results were then compared with BIA results from the Sri Lankan subjects derived from a different BIA device.

2.11 | Ethical clearances

Ethics clearance for the screening of Sri Lankan school children’s nutritional status in Negombo was obtained from the Ethical Review Committee of the Sri Lanka College of Pediatricians (SLCP). Ethical approval for the following metabolic screening of children with obesity connected to the screening process for a Metformin trial was obtained from the Ethics Review Committee of Faculty of Medicine, University of Colombo (EC-13-143). Only subjects with informed and written consent were included in the study.

All protocols and examinations performed on the Swedish subjects within the ULSCO cohort have been approved by the Uppsala Regional Ethics Committee (registration numbers 2010/036 and 2012/318). Informed and written consent is obtained from legal guardians, and for subjects ≥12 years of age, written consent is also obtained from the subjects themselves. Participation in the cohort is voluntary, and consent can be withdrawn at any time by subjects and legal guardians without having to state a reason.

2.12 | Statistical analysis

Statistical analysis was performed using the software IBM SPSS statistics version 25. Continuous variables are presented as mean values with SD. For comparison of two sample means, Student independent t test was used when test criteria for parametric testing was fulfilled, otherwise the non-parametric Independent-Samples Mann-Whitney U test was performed. For comparison of means between the five groups representing different states of glucose intolerance, one-way ANOVA with post-hoc analysis and the non-parametric Kruskal-Wallis test were performed. Correlations between parameters were calculated with Pearson bivariate correlation analysis and correlation coefficient along with the P-value is presented. Univariate logistic regression was used to study relation between the dependent variable (IGT/DM) and independent variables. A multivariate logistic regression model was then used to calculate the Odds ratios of different
covariates regarding to the risk of having IGT/DM or IFG. P values <.05 were considered statistically significant.

3 | RESULTS

3.1 | Characteristics of the Sri Lankan study population according to state of glucose intolerance

Of the 357 subjects included, 51.8% (n = 185) were boys and 48.2% (n = 172) were girls. Mean age was 11.9 years (±2.32 SD) and mean BMI-SDS was 2.6 (±0.44 SD).

OGTT results showed that 77.5% (n = 276) of the subjects had normal glucose tolerance (NGT). Isolated impaired fasting glucose (iso-IFG) was present in 9.0% (n = 32) and isolated impaired glucose tolerance (iso-IGT) in 8.4% (n = 30) of the subjects. Combined IFG + IGT was present in 3.1% (n = 11) and T2DM in 2.0% (n = 7) of the subjects (Figure 2A). One of the subjects fulfilled diabetes criteria defined only by elevated FG of 127 mg/dL, but did not fulfill diabetes criteria defined by 2-hours-glucose. Out of the other six subjects with T2DM, three had IFG and three NFG. Six out of seven diabetic subjects had started pubertal development, and even the prevalence of iso-IFG, iso-IGT and comb IFG + IGT was higher among pubertal and post-pubertal subjects than among pre-pubertal subjects (Figure 2B).

Mean values of anthropometric measures and laboratory parameters in the whole Sri Lankan study population and according to state of glucose intolerance are shown in Table 1 and illustrated for some parameters in Figure 3.

3.2 | Correlations between 2-hours-insulin and 2-hours-glucose according to state of glucose intolerance

There was a significant positive correlation between 2-hours-insulin and 2-hours-glucose in the whole Sri Lankan study population. When analyzed only for the groups with normal 2-hours-glucose (NGT and iso-IFG), the positive correlation between 2-hours-insulin and 2-hours-glucose was still significant (Figure 4A). In the groups with elevated 2-hours-glucose (iso-IGT, comb IFG + IGT, T2DM), there was no significant correlation between 2-hours-insulin and 2-hours-glucose.

**FIGURE 2** Distribution of different states of glucose intolerance within the whole Sri Lankan study population, A; and according to pubertal development, B, in percent
| TABLE 1  | Anthropometric measures and laboratory parameters (expressed as mean values ± SD) in the whole Sri Lankan study population (total) and according to state of glucose intolerance |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|           | Total (n = 357) | NGT (n = 276) | Iso-IFG (n = 32) | Iso-IGT (n = 30) | Comb IFG + IGT (n = 11) | T2DM (n = 7) | Overall P-value |
| Agea (years) | 11.90 (±2.32) | 11.76 (±2.33) | 11.69 (±2.56) | 12.87 (±1.87) | 12.82 (±1.47) | 13.29 (±1.98) | <.05 |
| BMI-SDS (WHO) | 2.61 (±0.44) | 2.61 (±0.45) | 2.58 (±0.49) | 2.66 (±0.36) | 2.48 (±0.28) | 2.74 (±0.40) | .70 |
| Waist-height-ratiob,c(WHR) | 0.58 (±0.04) | 0.58 (±0.04) | 0.57 (±0.03) | 0.60 (±0.05) | 0.58 (±0.03) | 0.60 (±0.08) | <.05 |
| BIA Total body fat (% of body weight) | 42.80 (±5.05) | 42.59 (±5.03) | 43.45 (±5.48) | 43.98 (±4.70) | 41.61 (±5.12) | 44.00 (±5.32) | .46 |
| Fasting glucoseb,c,d,e,f,g,h (FG, mg/dL) | 88.60 (±10.61) | 85.59 (±6.95) | 103.97 (±3.66) | 86.79 (±6.95) | 107.69 (±4.00) | 115.83 (±30.14) | <.0001 |
| 2 hours-glucoseb,c,d,e,f,g,i (2 hours-G, mg/dL) | 116.77 (±27.69) | 108.61 (±13.61) | 113.38 (±12.50) | 152.46 (±11.75) | 159.35 (±15.44) | 234.36 (±77.79) | <.0001 |
| Fasting insulina,b (FI, µIU/mL) | 17.93 (±30.10) | 16.91 (±27.65) | 26.36 (±36.83) | 17.49 (±8.21) | 20.47 (±22.74) | 18.09 (±8.39) | <.01 |
| 2 hours-Insulina,b (2 hours-l, µIU/mL) | 80.63 (±64.97) | 73.00 (±54.99) | 50.48 (±47.23) | 153.76 (±81.97) | 141.42 (±96.93) | 131.05 (±100.93) | <.0001 |
| HOMA-IRa | 3.93 (±6.65) | 3.55 (±5.64) | 6.62 (±14.03) | 3.71 (±1.70) | 5.39 (±5.71) | 5.28 (±2.94) | <.01 |
| Total cholesterol (TC, mg/dL) | 213.08 (±42.07) | 212.07 (±42.78) | 218.18 (±33.01) | 210.28 (±40.66) | 218.59 (±58.57) | 233.11 (±27.31) | .64 |
| LDL-cholesterol (LDL, mg/dL) | 130.83 (±35.26) | 129.87 (±36.41) | 137.42 (±23.14) | 126.98 (±31.07) | 136.10 (±50.03) | 147.14 (±21.66) | .49 |
| HDL-cholesterol (HDL, mg/dL) | 52.94 (±12.29) | 53.14 (±12.64) | 52.25 (±11.15) | 52.57 (±12.71) | 50.09 (±7.38) | 53.86 (±9.37) | .94 |
| Triglycerides (TG, mg/dL) | 146.45 (±49.14) | 145.14 (±49.39) | 142.59 (±41.81) | 153.67 (±56.93) | 162.02 (±47.62) | 160.57 (±38.40) | .61 |
| hs CRP (mg/dL) | 1.14 (±0.85) | 1.16 (±0.89) | 1.03 (±0.73) | 1.03 (±0.66) | 1.03 (±0.57) | 1.63 (±1.13) | .46 |
| ALT = GPT (U/L) | 30.39 (±24.99) | 30.09 (±26.43) | 27.30 (±17.16) | 35.50 (±23.75) | 30.98 (±15.38) | 33.40 (±10.28) | .76 |
| AST = GOT (U/L) | 25.44 (±12.99) | 25.54 (±13.53) | 23.45 (±8.83) | 27.11 (±14.22) | 24.11 (±9.15) | 25.14 (±9.94) | .85 |
| SBPd,i | 106.75 (±11.08) | 106.24 (±10.27) | 104.06 (±8.65) | 109.83 (±9.51) | 114.55 (±27.34) | 112.86 (±10.75) | <.05 |
| DBP | 66.48 (±10.18) | 66.41 (±7.94) | 65.94 (±7.87) | 66.00 (±8.65) | 67.73 (±11.26) | 70.00 (±7.64) | .76 |
| SDS_SBP | −0.62 (±1.04) | −0.64 (±1.03) | −0.86 (±0.80) | −0.41 (±0.87) | −0.14 (±2.12) | −0.23 (±0.86) | .16 |
| SDS_DBP | 1.12 (±0.91) | 1.12 (±0.90) | 1.06 (±0.89) | 1.03 (±0.93) | 1.22 (±1.27) | 1.49 (±0.84) | .80 |

Note: Significant differences between groups.

'aNGT/iso-IFG.
bNGT/iso-IGT.
cNGT/comb IFG + IGT.
dNGT/T2DM.
eISO-IFG/iso-IGT.
fISO-IFG/comb IFG + IGT.
gISO-IFG/T2DM.
hISO-IGT/comb IFG + IGT.
iISO-IGT/T2DM.
jComb IFG + IGT/T2DM.
glucose, and individuals with the highest values of 2-hours-glucose tended to have lower values of 2-hours-insulin (Figure 4B).

### 3.3 Prevalence of other obesity comorbidities in the Sri Lankan study population according to state of glucose intolerance

As shown in Table 1, mean values of certain markers of obesity comorbidities differed between the five groups representing different states of glucose intolerance. The most common comorbidity in this study population was acanthosis nigricans with a prevalence of 85.7% in the whole cohort and quite equal distribution between the different states of glucose intolerance. Other comorbidities with high prevalence were insulin resistance defined by elevated HOMA-IR with a prevalence of 52.9% in the whole cohort (highest prevalence in the iso-IGT group with 85.2%) and elevated total cholesterol with a prevalence of 29.2% in the whole cohort (highest prevalence in the comb IFG + IGT group with 45.5%). Whereas 34.5% of the subjects in this study showed increased echogenicity determined by ultrasound scan of the liver, only 17.7% had elevated values of the liver enzyme ALT. Figure 5A shows the prevalence of different obesity comorbidities in percent in each group according to cut-off-values presented in the methods section. Figure 5B illustrates the cumulative prevalence of all different obesity comorbidities that seems to increase from NGT over iso-IFG, iso-IGT, comb IFG + IGT to T2DM.

### 3.4 Association of risk factors with different states of glucose intolerance

Bivariate correlation analysis showed that 2 hours-G correlated positively with age, puberty, WHtR, fasting glucose and 2-hour-insulin, but also with family history of diabetes and educational status of the father. It did not correlate directly with educational status of the mother, even if educational status of the mother was correlated to educational status of the father and thereby showed an indirect correlation. 2-hours-G did not correlate with fasting insulin, liver enzymes or blood lipids, and neither with BMI-SDS, total body fat mass or waist-hip-ratio. There was no significant correlation between grade of NAFLD and state of glucose intolerance.
In a multivariate logistic regression model, three variables (FG, 2 hours-I and educational status of the father) independently increased the Odds ratio to have IGT or diabetes. When corrected for age, puberty, sex, WHtR and family history of diabetes, FG increased the Odds ratio to have IGT or diabetes with OR = 1.09 (95% CI: 1.05-1.14, \(P < .0001\)), 2 hours-I with OR = 1.01 (95% CI: 1.01-1.02, \(P < .0001\)) and educational status of the father with OR = 5.60 (95% CI: 2.21-14.18, \(P < .0001\)). All three variables still significantly increased the Odds ratio to have IGT or diabetes when diabetic subjects were excluded. Out of the five factors adjusted for (age, puberty, sex, WHtR and family history of diabetes), age had the strongest impact on development of IGT or diabetes with OR = 1.23 (95% CI: 1.01-1.50, \(P < .05\)). Pubertal stage did not significantly increase the Odds ratio for IGT or diabetes.

Comparison of means showed that subjects whose father had higher educational status had significantly higher mean 2 hours-G (122.7 mg/dL ± 34.0 SD) during OGTT compared with subjects whose father had lower educational status (112.2 mg/dL ± 21.0 SD, \(P = .001\)). There was no significant difference in mean BMI-SDS between the two groups. There was no significant difference in mean 2 hours-G or mean BMI-SDS between groups with different family income or different educational status of the mother.

FG correlated positively with 2 hours-G, age and pubertal stage. It showed a negative correlation with HDL.

### 3.5 | Comparison with Swedish study population

For comparison of fat distribution and risk profile at the same degree of obesity, 167 of the Sri Lankan subjects were matched for sex, BMI-SDS and approximate age with 167 Swedish subjects from the ULSCO cohort. At both sites, the study population included for
comparison consisted of 95 boys and 72 girls. There was no significant difference in mean BMI-SDS or mean age between the Sri Lankan and the Swedish subjects included for comparison. The group of 167 Sri Lankan subjects had significantly higher amount of body fat in %, but lower WHtR compared with 167 Swedish subjects with similar BMI-SDS, age and sex distribution. The Sri Lankan subjects also had higher total cholesterol, LDL, HDL and triglycerides, but there was no significant difference in TC/HDL-ratio or LDL/HDL-ratio between the two groups. Sri Lankan subjects had lower glucose and insulin levels both fasting and 2 hours after glucose load during OGTT, and lower HOMA-IR. Acanthosis nigricans was much more common in Sri Lankan subjects than in Swedish subjects (Table 2).
3.6 Discussion

The present study shows that Sri Lankan children with obesity have relatively high prevalence of glucose intolerance, and thereby confirms the findings from another recent study in Sri Lankan children and adolescents with obesity. The prevalence of IFG in the present study population was 12.1% according to ADA criteria and the prevalence of IGT was 11.5%. These numbers are comparable with prevalence numbers reported from European and other industrialized countries, but also with findings from previous studies in South Asian...
children and adolescents. At the same time, the prevalence of childhood overweight and obesity is still lower in Sri Lanka compared to most industrialized countries. A possible explanation for the finding that Sri Lankan children with obesity have a comparable prevalence of comorbidities at a lower mean degree of obesity could be that they have a higher vulnerability to obesity related complications compared with other ethnic groups.

To be able to distinguish different forms of glucose intolerance and analyze characteristics of subjects presenting the different forms, subjects in this study were divided into five groups, representing five different states of glucose intolerance from normal glucose tolerance (NGT) over isolated impaired fasting glucose (iso-IFG), isolated impaired glucose tolerance (iso-IGT) and combined IFG + IGT (comb IFG + IGT) to type 2 diabetes mellitus (T2DM). All states of glucose intolerance (besides NGT) were more common in pubertal and post-pubertal subjects than in prepubertal subjects (Figure 2B). Furthermore, there was an increase in mean age between the five groups in the mentioned order (Figure 3A) indicating a possible progression during childhood and adolescence from NGT over the isolated and then combined forms of IFG and IGT to T2DM. Even if age showed a positive correlation with more advanced states of glucose intolerance, and significantly increased the Odds ratio to have IGT or diabetes, the present study was not able to statistically define a cut-off age for screening for glucose intolerance, which might depend on the low number of subjects in the younger age groups. Nevertheless, there were no cases of IGT under the age of 9 years, and the first cases of combined IFG + IGT and diabetes occurred at the age of 10 years in this sample. This might lead to the suggestion to recommend screening for glucose intolerance from the age of approximately 10 years, which then should be validated in a larger sample also including more subjects in the younger age groups. The fact that other variables (eg, family history of diabetes and educational level of the father) had greater impact on the risk of developing IGT or diabetes than age in this study illustrates the multifactorial genesis of obesity itself and its comorbidities, leading to difficulties in defining simple and easy accessible fasting parameters for the selection of subjects that should undergo the more elaborate OGTT to screen for glucose intolerance. Whereas there was a positive correlation between 2 hours-G and 2 hours-l in the groups with normal 2 hours-G (NGT and iso-IFG, Figure 4A), this correlation could no longer be found in the groups with elevated 2 hours-G (iso-IGT, comb IFG + IGT and T2DM, Figure 4B). Furthermore, in subjects with the highest values of 2 hours-G, levels of 2 hours-l showed a trend to decrease with increasing levels of 2 hours-G. One possible explanation for this finding might be that it reflects the capacity of the beta-cell to respond to increasing glucose levels with increased insulin production, showing that the beta-cell has efficient capacity to compensate for increasing levels of 2 hours-G in the lower states of glucose intolerance, whereas the capacity starts to decline in the more advanced states of glucose intolerance (mainly comb IFG + IGT and T2DM). The finding that the cumulative prevalence of different obesity comorbidities seems to increase from NGT over iso-IFG, iso-IGT, comb IFG + IGT to T2DM (Figure 5) is another indicator that these five states of glucose intolerance in the mentioned order might reflect progression of disease.

In the present study, the risk to have come further in the progress of disease and to present a more advanced state of glucose intolerance was not only determined by age, but also by educational status of the father. Previous studies have found that overweight and obesity are more prevalent among lower socioeconomic groups in industrialized countries, whereas the prevalence of overweight and obesity is higher in higher socioeconomic groups in developing countries. In the present study, there was no significant difference in the prevalence of obesity itself between different socioeconomic groups, but the level of education of the father correlated positively with glucose levels at 2 hours of OGTT. Furthermore, the risk of having IGT or diabetes was higher for children to parents with higher educational level compared with those with lower educational level. These findings indicate that the risk for certain metabolic complications of obesity is higher for individuals belonging to higher socioeconomic groups in Sri Lanka, as well as in other developing countries.

The prevalence of hypercholesterolemia was high with 62.7% in this study population of Sri Lankan children with obesity, and has been described to be relatively high even in normal weight Sri Lankan school children. Whereas 34.5% of the subjects in this study showed increased echogenicity determined by ultrasound scan of the liver, only 17.7% had elevated values of the liver enzyme ALT (Figure 5). This indicates a discrepancy in the estimation of liver steatosis depending on the method chosen. However, prevalence numbers of different comorbidities should be interpreted with caution, taking into account that different reference values are used in different countries and that reference values often are generated from studies in adults.

The present study confirmed findings from previous studies claiming that Sri Lankan children with obesity have higher amount of body fat compared with children of other origin with the same degree of obesity. The fact that Sri Lankan children in the present study not only had higher percentage of total body fat than Swedish children with the same degree of obesity, but lower WHTr at the same time indicates that they have a different fat distribution with lower amount of abdominal fat. Compared with Swedish children, Sri Lankan children with obesity had higher levels of total cholesterol, LDL and triglycerides, but even HDL cholesterol. They also had lower HOMA, which indicates a lower degree of insulin resistance in Sri Lankan children compared with Swedish children. Caution should be exerted in interpreting these results, as Swedish subjects included in the ULSCO cohort are referred from other caregivers and thereby likely to have received previous treatment for obesity, whereas subjects at the Sri Lanka study site were included from a school screening without any previous treatment for obesity. Furthermore, it should be taken into account that blood samples were taken at two different centres and analyzed under different conditions. Also, the use of different BIA devices for measuring body composition is a potential limitation of the study, as it might lead to inaccuracy in the comparison of subjects from the two different sites.
Further studies under more standardized conditions are needed to explain which of the factors testing conditions, referral routines, different lifestyle parameters or biological factors that have the strongest impact on the observed differences in body composition and prevalence of comorbidities between South Asian and European children and adolescents with obesity.

Nevertheless, differences in blood indicators of comorbidities between South Asian and European children have been described in other studies. One previous study compared British children of South Asian origin with white children and found that mean waist circumference and waist-hip-ratio were similar, but South Asian children had higher triglycerides and insulin levels (both fasting and after glucose load), though glucose concentrations were similar. Total cholesterol, LDL and HDL levels were similar in the two groups in the same load), though glucose concentrations were similar. Total cholesterol, LDL and HDL levels were similar in the two groups in the same load). The results of the present study only partly confirm these findings and other findings from previous literature comparing South Asian children with children of other ethnic origin, as Sri Lankan children in this study showed higher amount of total body fat and higher levels of blood lipids, but lower degree of abdominal obesity and insulin resistance compared with Swedish children. Discrepancies in results from studies comparing prevalence of different comorbidities in children with obesity and different ethnic backgrounds indicate a need of future multicentre studies with well harmonized study settings.

Besides potential differences in laboratory methods between the Sri Lankan and the Swedish study site, another weakness of the present study is that only subjects with BMI-SDS >2 were considered having obesity, as recent data shows that lower cut-offs might be recommended in Sri Lankan children. Furthermore, there was a time gap of up to 14 months between the school screening and the biochemical assessments at the centre. Even if anthropometric measurements were conducted at both events, lifestyle patterns such as physical activity and nutritional habits were only evaluated at screening and might have changed until the assessments at the centre, possibly even due to the knowledge of the child having obesity.

Nevertheless, the present study is one of the first to present data on glucose intolerance in a bigger sample of Sri Lankan children and adolescents with obesity, and it provides detailed information not only on metabolic and anthropometric, but also on socioeconomic and lifestyle parameters. Furthermore, it adds knowledge about the metabolic risk profile of Sri Lankan children and adolescents in comparison with Swedish children and adolescents with the same degree of obesity. The fact that glucose intolerance was common in Sri Lankan children and adolescents with obesity in this study, and that other risk factors besides age increased the risk of having more advanced states of glucose intolerance, indicates that screening for glucose intolerance is important even in asymptomatic subjects to avoid progression to T2DM.

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Conflict of Interest
The authors declare no potential conflict of interest.

Author Contributions
Loretta S. Warnakulasuriya, Adikaram V. N. Adikaram, Manel M. A. Fernando, Dulani L. Samaranyake, K. D. Renuka Ruchira Silva, and V. Pujitha Wickramasinghe were involved in the planning and formation of the study at the Sri Lankan site in Negombo. Loretta S. Warnakulasuriya, Adikaram V. N. Adikaram, and Manel M. A. Fernando conducted and K. D. Renuka Ruchira Silva and V. Pujitha Wickramasinghe supervised the study. Elisabet Ryttener was involved in the planning and conduction of the Sri Lankan study on behalf of the Swedish Radiohjälpen “Children of the World” and Lions Sweden. Iris Ciba, Peter Bergsten, Marie Dahlbom, and Anders H. Forslund were involved in the planning and formation of the Uppsala Longitudinal Study of Childhood Obesity (ULSCO). Iris Ciba analyzed the data and drafted the manuscript. Loretta S. Warnakulasuriya, Peter Bergsten, Marie Dahlbom, Elisabet Ryttener, V. Pujitha Wickramasinghe, and Anders H. Forslund coauthored, revised, and critically reviewed the final manuscript as submitted. All authors have critically reviewed and approved the final manuscript as submitted.

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Ethics Statement
Ethics clearance for the screening of Sri Lankan school children's nutritional status in Negombo was obtained from the Ethical Review Committee of the Sri Lanka College of Pediatricians (SLCP). Ethical approval for the following metabolic screening of children with obesity connected to the screening process for a Metformin trial was obtained from the Ethics Review Committee of Faculty of Medicine,
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