

Validation of Equations for the Prediction of Resting Metabolic Rate in Sri Lankan Adults

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Abstract- ‘Desktop’ indirect calorimetry has been demonstrated to be a robust alternative to the traditional ‘metabolic cart’ indirect calorimetry in the measurement of resting metabolic rate (RMR) and can be used effectively for the validation of RMR prediction equations. RMR prediction equations need to be population specific due to ethnic variation in body composition. Currently, RMR equations validated against a reference method do not exist for Sri Lankans. This study was designed to validate existing RMR equations against a reference method, indirect calorimetry, in healthy Sri Lankans. Data from fifty-seven healthy Sri Lankans (27 males and 30 females) aged 19-60 years were included in this cross-sectional study. RMR was measured by indirect calorimetry and also predicted using available RMR equations. A predicted RMR (RMR_p) that was within $\pm 10\%$ of RMR measured (RMR_m) was considered an accurate prediction. Validity of the equations was assessed by paired t-test and Bland Altman analysis. Correlation between RMR_m and RMR_p was assessed by Pearson correlation. RMR_p by all equations varied more than 10% from the RMR_m. Existing RMR equations are not suitable for the Sri Lankan population. A new population specific equation needs to be developed for Sri Lankans.

Index Terms- Resting Metabolic Rate, Indirect Calorimeter, Sri Lankan adults

I. INTRODUCTION

Prevalence of overweight and obesity are rising in Sri Lanka [1]. Obesity causes increased risk of several diseases including cardiovascular disease, diabetes mellitus and non alcoholic fatty liver disease [2]. Even though the aetiology of obesity is complex and influenced by many factors, many studies have shown that persistent positive energy balance increases susceptibility to metabolic diseases [3]. Energy balance is important in weight management. Energy balance is achieved when energy intake is equal to energy expenditure [4]. Energy intake varies with many factors including food availability, food quality, personal preference and serving size. When energy intake exceeds the energy expenditure, this excess energy is deposited as fat in the body leading to increased body weight [5]. Total energy expenditure (TEE) is the total number of calories used up by an individual per day and doubly labeled water method is the gold-standard to measure TEE [6]. TEE can be broadly divided into three categories. They are basal metabolic rate/resting metabolic

rate, thermic effect of food and physical activity energy expenditure [7].

Resting metabolic rate (RMR) is the energy requirement of an individual at complete rest. The definition of RMR can be further refined as the amount of energy expended when the individual is awake in a supine position in a post-absorptive, thermo-neutral state while having not exercised for typically 12 hours and fasted for 10-12 hours [8]. It includes normal body function at rest such as berating, cardiovascular function and brain function. It is slightly higher than basal metabolic rate, which is the minimum energy requirement to sustain life [9]. Practically, RMR is more useful in estimating total energy expenditure and better reflects the real life scenario than BMR [8]. RMR is the largest component of TEE and therefore provides baseline values for the estimation of calorie needs in clinical practice. It is used as a base, and together with activity factors is used to calculate energy requirement when designing diets and exercise schedules in weight management [10].

The gold-standard method to measure RMR is direct calorimetry and it uses the law of energy conversion. The rate at which heat is produced by body when burning a fuel is a direct reflection of metabolism and is proportional to the metabolic rate. Therefore, measuring the body's heat production gives a direct measure of metabolism [11]. This procedure requires a specialized room and technology to measure heat production. Although theoretically direct calorimetry would be the most accurate way to measure metabolic rate, it is not always practical to perform in day to day clinical settings as the equipment needed is complex, expensive, and the procedure is time-consuming placing a heavy burden on the participant [6]. Direct calorimeters are available only in a very few centers in the world.

Indirect calorimetry (IC), reference method measures energy expenditure not through the heat produced but by measuring the volumes of respiratory gases exchange, using the metabolic cart. Thus IC is an indirect measure of metabolism. The metabolic cart measures the volume of oxygen used and the volume of carbon dioxide produced by the body, and through this, calculates the energy used by the body when metabolizing the major fuels using the Weir (1949) equation [12]. The desktop indirect calorimeter is a robust alternative to the traditional metabolic cart. Desktop indirect calorimeters use the fixed 0.85 respiratory quotient (RQ) as the default setting to calculate energy expenditure using the modified Weir equation [10]. FitMate, desktop indirect calorimeter used in present study is a reliable and

valid system for measuring RMR compared to Douglas bag and metabolic cart measurements [13, 14].

RMR measurements using both direct and indirect calorimetry require strictly controlled conditions before and during the measurement as RMR can be influenced by many factors such as room temperature, time of the day, food intake, physical activity and medication [15]. Hence at field level, calorimetric measurement of RMR is often replaced by prediction equations. RMR prediction equations have been developed and validated in different populations based on easily measured variables such as weight, height, age, gender and body composition [7]. Ethnic variations exist in body composition. Asians have greater amount of body fat for a given BMI, as well as being at a greater risk of obesity at lower BMI than global cut-offs [1]. RMR prediction equations have been developed and validated predominantly on Western populations [9]. Prediction equations developed in these populations are known to have poor validity in other populations [9, 16, 17]. Validation of existing RMR equations against a reference method before using them in a population, other than which it was developed, is a prerequisite to ensure accuracy in estimating RMR. Only a few equations have been developed in Asians and they have not been validated in the Sri Lankan population. Our aim was to validate existing published equations for the assessment of RMR in healthy Sri Lankan adults, against the indirect calorimetry method.

II. METHODOLOGY

Participants

A total of 59 apparently healthy Sri Lankans (29 males and 30 females) aged between 19 and 60 years residing in Colombo area were recruited to this cross-sectional study. Sample size was calculated according to Liao [18] method for an agreement study. Exclusion criteria included pregnant or lactating mothers, a change in body weight greater than 5% over the past 6 months, an attempt to lose weight through dieting over the past three months, major illness or on medication including anti-obesity medication and bariatric surgery. Smokers, alcohol consumption within the past 8-10 hours, physical exercise over the preceding 12 hours prior to procedure and females in their menstruation days were also excluded. This study was carried out at the Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Colombo, Sri Lanka.

Ethics

Ethics Review Committee of the Faculty of Medicine, University of Colombo, approved the study protocol and all procedures followed were in accordance with the ethics standards

of this committee. All participants were explained about the study protocol and informed written consent was obtained.

Anthropometric Measurements

Anthropometric measurements (weight and height) were taken from each volunteer on the test day using the same equipment in order to minimize variability. Weight was measured to the nearest 0.1kg using a calibrated electronic scale (Seca 803) and height was measured to the nearest 0.1cm using a stadiometer (Seca 225, telescopic height measurement) using standard protocol.

RMR measurement using the ventilated hood indirect calorimeter (RMRm)

RMR was measured between 8.00 am and 10.00 am using a desktop indirect calorimeter with ventilated hood (COSMED Fitmate GS[®], Italy) which was calibrated before each test. Measurements were performed after an overnight fast of at least 10 hours. Participants were advised to refrain from intensive physical activity for a minimum of 12 hours prior to the measurement and to abstain from coffee and other nicotine containing food or beverage, heavy meals, smoking and alcohol on the evening prior to measurement.

Participants were rested for 20 minutes, in a supine position while being awake prior to the test. Measurements were performed in a quiet, thermo-neutral (~25°C) environment. Once the 20 minute resting period was completed resting metabolic rate was measured, using the ventilated hood system. The modified Weir equation, with a respiratory quotient (RQ) of 0.85 was used to calculate the RMR [10]. Duplicate RMR measurements were taken on two different days from each participant.

Predicted RMR by equations (RMRp)

Ten equations were used to predict RMR; Harris-Benedict [19], Schofield [20], WHO_{weight} [21], WHO_{height & weight} [21], Owen [22, 23], Mifflin St Jeor [24], Henry [9], Liu [16], Ganpule [25] and Indian equations [26, 27]. These equations only use easily measurable variables such as height, weight, age and gender as their predictive variables. Equations used in this study are summarized in Table 1.

Statistical Analysis

The data was analyzed using SPSS Statistics software (version 21.0). The following tests were conducted to determine the validity of predicted RMR (RMRp) using pre-existing equations against measured RMR (RMRm) using the indirect calorimeter (ventilated hood). Pearson correlation coefficient was used to assess the association between RMRm and RMRp. Paired t-test was used

Table 1: Selected RMR prediction equations

Equation	Reference	Population to which the equation was derived
Male RMR=66.473+(13.752xW)+(5.003xH)-(6.755xA) Female RMR=655.096+(9.563xW)+(1.850xH)-(4.676xA)	Kcal/day Harris & Benedict [19] 1918	N=239 , 21-70 years USA
Male18-30y: RMR= (15.1xW)+692 30-60y:RMR=(11.5xW)+873 Female18-30y: RMR =(14.8xW)+487 30-60y:RMR=(8.3xW)+846	Kcal/day Schofield [20] 1985	N=7,173, >18 years Mostly Europeans and Americans
Male18-30y: RMR=(15.3 x W) +679 30-60y: RMR=(11.6xW)+879 Female18-30y: RMR=(14.7xW)+496 30-60y: RMR=(8.7xW)+829	Kcal/day FAO/WHO/UNU [21] 1985	based on Schofield's work
Male 18-30y:RMR=(15.4xW)-(27xHM)+717 30-60y:RMR=(11.3xW)-(16xHM)+901 Female 18-30y:RMR=(13.3xW)+(334xHM)+35 30-60y:RMR=(8.7xW)-(25xHM)+865		
Male RMR=(Wx10.2)+879 Female RMR=(Wx7.18)+795	Kcal/day Owen <i>et al</i> [22, 23] 1986	N=104 , 18-82 years, USA
RMR=(9.99xW)+(6.25xH)-(4.92xA)+(166xSEX)-161	Kcal/day Mifflin <i>et al</i> [24] 1990	N=498, 19-78years, USA
Male18-30y: RMR=(16.0xW)+545 30-60y:RMR=(14.2xW)+593 Female18.0-30y:RMR=(13.1xW)+558 30-60y: RMR=(9.74xW)+694	Kcal/day Henry [9] 2005	N=10,552 (From Oxford data base)
Male RMR=(13.88xW)+(4.16xH)-(3.43xA) Female RMR=(13.88xW)+(4.16xH)-(3.43xA)-112.4	Kcal/day Liu <i>et al</i> [16] 1995	N=223, 20-78 yeras Chinese
Male RMR=(0.0481xW)+(0.0234xH)-(0.0138xA)-0.425 Female RMR=(0.0481xW)+(0.0234xH)-(0.0138xA)-0.9708	MJ/day Ganpule <i>et al</i> [25] 2007	N=137 Japanese
Male RMR=(48.7xW)+(14.1xA)+3599 Female RMR=(45.6xW)+2479.7	KJ/day Soares <i>et al</i> [26] 1993 Piers & Shetty [27] 1993	N=121 males, 18-30 years Indian N=60 females , 18-30 years Indian

A, Age; W, weight; H, height in centimeters; HM, height in meters; Sex F=0 M=1

to examine the mean difference between RMR_m and RMR_p at group level for each equation. Overestimation and underestimation at group level were estimated using the direction of the mean difference.

The degree of agreement and the systematic bias between RMR_m and RMR_p were evaluated by Bland-Altman limits of agreement analysis. The limits of agreement were defined as the mean difference ± 1.96 standard deviation [28]. The percentage

bias at individual level was calculated by the percentage difference [(RMR_p-RMR_m) /

RMR_m x 100] or error, for each participant.

Table 2: General characteristics of the participants.

	Total	Male	Female
	(n=57)	(n=27)	(n=30)
Age (years)	34.88 (13.05)	33.56 (12.12)	36.07 (13.93)
Weight (kg)	62.57 (10.37)	67.26 (11.07)	58.34 (7.66)
Height (cm)	162.11 (8.69)	168.59 (6.33)	156.26 (5.95)
BMI (kg/m ²)	23.74 (2.86)	23.56 (2.90)	23.89 (2.86)
RMR (kcal/day)	1169.6 (184.7)	1291.3 (165.6)	1060.2 (122.9)

Data are presented as mean (standard deviation), BMI-body mass index

An accurate prediction (acceptable error) at individual level was defined as a value for RMRp which fell within $\pm 10\%$ of RMRm [29]. The proportion of participants with acceptable error as well as those with over-predicted and under-predicted RMRp also were calculated. Significance was set at $p < 0.05$.

III. RESULTS

Fifty seven participants completed the study and were included in the final analysis. Of the fifty nine participants who

initially signed the consent form, two participants did not follow up RMR measurements on second day. The general characteristics of the population are given in Table 2.

The sample comprised of 53% female (n=30) and 47% male (n=27) subjects. The mean BMI was 23.9 kg/m² (SD=2.9) for females and 23.6 kg/m² (SD=2.90) for males. Mean measured RMR was 1060 kcal/day (SD=123) for females and 1291 kcal/day (SD=166) for males.

Mean RMR values measured using indirect calorimetry and estimated using prediction equations are listed in Table 3. Predicted RMR values using existing prediction equations were significantly higher than RMR measured by the reference method (indirect calorimetry).

Mean difference between RMRm and RMRp was assessed by paired t-test and results indicated that these prediction equations led to a significant ($p < 0.05$) overestimation of measured RMR in Sri Lankan adults. Paired T-test results are shown in Table 3. Correlation between RMRm and RMRp was analyzed by Pearson correlation. All RMRp values strongly correlated with RMRm as shown in Table 3.

A Bland-Altman plot was created for each equation (10 equations) to assess the systematic bias between RMRm and RMRp and to generate the limits of agreement (mean bias ± 1.96 x standard deviations, 95%). Figure 1 shows the Bland-Altman plots of the difference between RMRm and RMRp against the RMRm measured by the indirect calorimeter (reference method). All the equations showed a wide limit of agreement, as well as directional bias where predicted values were always higher than measured values. Though falling within limits, the wide limits indicate poor agreement. The bias (mean difference between RMRm and RMRp) was negative for all the equations indicating overestimation.

Table 3 shows the mean bias at group level as well as at individual level through the % of participants who were correctly predicted and % of participants who were over predicted in relation to actual RMR values, calculated at individual level.

Table 3: Mean resting metabolic rate, Group bias, correlation, percentage of participants with accurate and over prediction in 57 Sri Lankan adults

Equation	Mean (SD) Kcal/day	Bias (SD) Kcal/day	R² Biases (P value)	SEE Kcal/day	Pearsons' correlation coefficient	% of accurate prediction ($\pm 10\%$ RMRm)	% of over prediction
Harris-Benedict [19]	1463.1 (200.5)	-293(108)*	0.019 (=0.303)	108	0.846**	5.2	94.8
Schofield [20]	1495.8 (205.2)	-326 (104)*	0.005 (=0.584)	105	0.863**	3.4	96.6
FAO/WHO/UNU [21] (weight)	1433.0 (181.3)	-263 (128)*	0.139 (=0.004)	120	0.754**	18.3	81.7

FAO/WHO/UNU [21] (height & weight)	1462.3 (195.1)	-293 (131)*	0.073 (=0.042)	127	0.764**	14.5	85.5
Owen <i>et al</i> [22, 23]	1389.2 (209.0)	-220 (115)*	0.007 (=0.573)	115	0.838**	20.4	79.6
Mifflin <i>et al</i> [24]	1384.2 (220.8)	-215 (121)*	0.000 (=0.988)	123	0.837**	22.1	77.9
Henry [9]	1425.2 (196.9)	-256 (96)*	0.016 (=0.349)	96	0.877**	10.2	89.8
Liu <i>et al</i> [16]	1421.5 (211.7)	-252 (100)*	0.000 (=0.892)	101	0.881**	8.5	91.5
Ganpule <i>et al</i> [25]	1340.0 (207.6)	-170 (102)*	0.001 (=0.784)	103	0.871**	34.6	65.4
Indian equations [26, 27]	1371.3 (185.1)	-202 (93)*	0.063 (=0.060)	79	0.870**	24.6	75.4

RMR, resting metabolic rate; *RMRm*, measured resting metabolic rate;

SEE-Standard error of estimate

*Significant overestimation from reference method ($p < 0.001$);

**significant correlation ($p < 0.001$);

Accurate prediction %- percentage of participants whose predicted values were $\pm 10\%$ of measure values

Over prediction %- percentage of participants whose RMR predicted values above 10% of measured values

These results show a low rate of accurate prediction and a high rate of over prediction by all prediction equations. None of the equations provided percentage bias $\leq -10\%$, at group level and at individual level, indicating that there was no under-prediction.

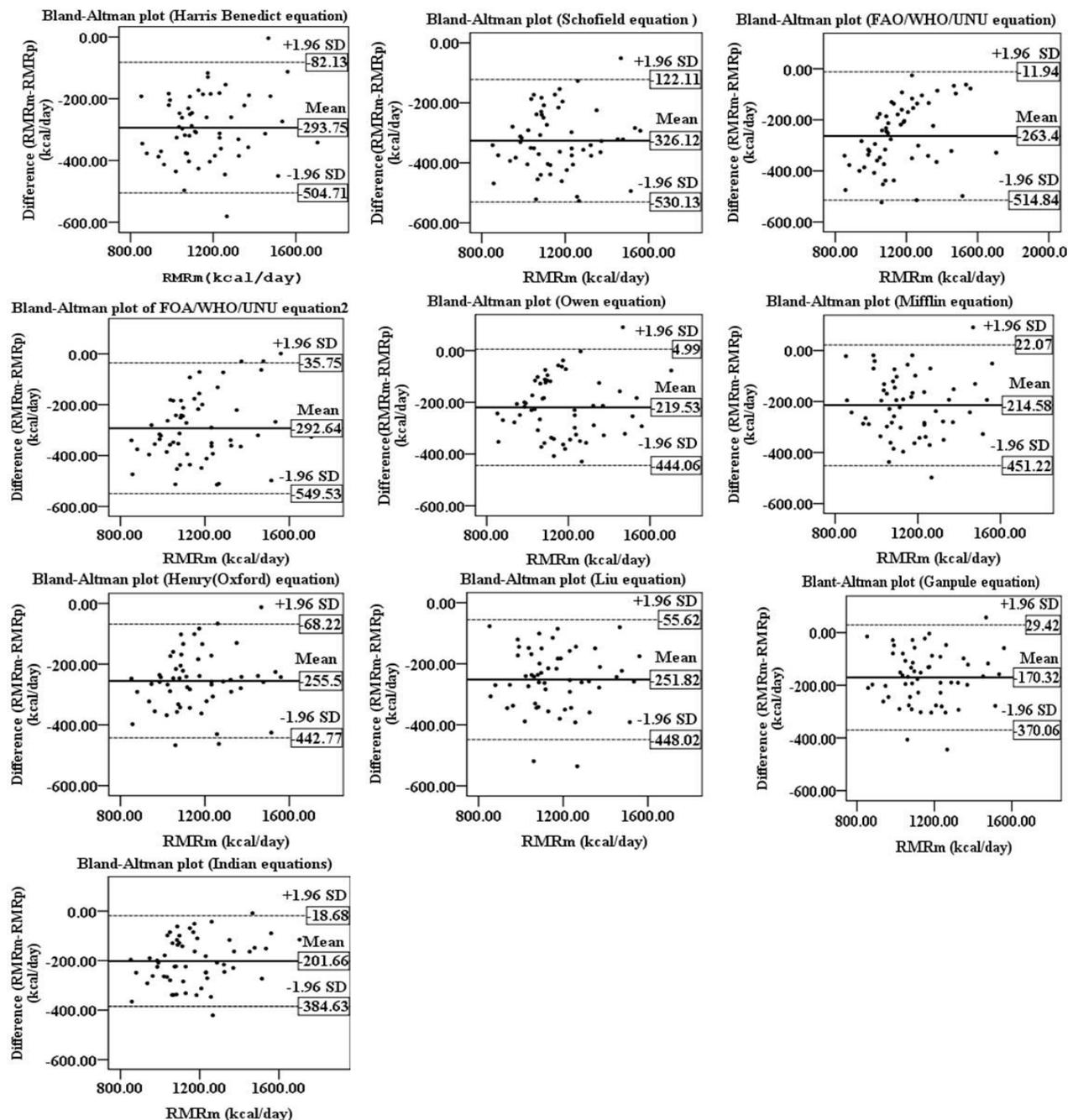


Figure 1: Plots of the bias between (RMR) determined by indirect calorimetry and by prediction equations against Measured RMR. The solid line is the mean measurement difference and dashed lines represent the upper agreement limit and the lower agreement limit.

IV. DISCUSSION

Persistent positive energy balance is a significant contributor to overweight and obesity. Both over and underestimation of RMR, result in poor estimation of total energy requirement and hamper the effectiveness of individualized nutrition therapy in weight management. We demonstrate for the first time that RMR equations developed in western populations perform poorly against indirect calorimetry, in Sri Lankans. The rising burden of obesity and non-communicable disease (NCD) in Sri Lanka emphasizes the need for accurate RMR estimation methods. The

current rate of obesity is 9.2% in Sri Lankan adults according to the proposed World Health Organization cut-off values for Asians [1]. The RMR values were normally distributed in the sample allowing valid comparisons to be made, with results being generalizable.

Our study demonstrates that predicted RMR values using commonly used equations are significantly ($p < 0.05$) higher than measured RMR. Harris Benedict equation is a widely used RMR equation globally [3]. This equation was developed over a century ago in an American population using indirect calorimetry. Two recent studies in Middle Eastern Asia reported that Harris

Benedict equation showed the highest accuracy in Jordanian females and Iranian females [3, 30]. RMR values in the present study population were overestimated by 293 ± 108 kcal/day. This finding is consistent with the findings of many other reports in Asia indicating that Harris-Benedict equation overestimates RMR values in Asians [7, 29].

Schofield and FAO/WHO/UNU equations are commonly used in Europe and Australia. Findings of the current study show that, there was a significant overestimation by Schofield and FAO/WHO/UNU equations in Sri Lankans. Schofield equation overestimated RMR in Sri Lankans by 326 ± 104 kcal/day. The inaccuracy of this equation in tropical populations has also been identified [9]. This issue was further highlighted in the FAO/WHO/UNU report as the same Schofield database was included here [17].

A South Asian study reported that FAO/WHO/UNU equation provides a good prediction for rural Bangladeshi women of 18-35 years [31]. In our study, FAO/WHO/UNU (weight) and (Weight & height) equations overestimated RMR by 263 ± 128 kcal/day and 293 ± 131 kcal/day respectively. This finding is consistent with the findings of many other reports in Asia [9, 17]. Maraki *et al.* [32] found that even RMR in Europeans (Greek pop

Henry [9] has suggested that over representation of Italians in the Schofield database may have caused the overestimation in RMR values in the tropics by Schofield and FAO/WHO/UNU equations [29]. Italians are known to have higher RMR among Europeans, which led to the exclusion of all Italians from the database in the development of the oxford equation also known as the Henry equation [9]. A larger number of RMR data from tropical regions was included in this database to improve the prediction accuracy in tropical populations [9]. Henry concluded that the Oxford equation was a better predictor of RMR in tropical populations including Asia. However Yang *et al* [17] reported that Henry equation overestimated RMR in normal weight Chinese adults. Hence it is not unexpected that Henry equation overestimated RMR by 255 ± 96 kcal/day in Sri Lankans.

The findings of this study demonstrate that Owen and Mifflin St Jeor equations overestimate RMR values in Sri Lankans by 220 ± 115 kcal/day and 215 ± 121 kcal/day respectively. However, these two equations better predicted RMR when compared to the other four widely used equations (H-B, Schofield, FAO/WHO/UNU and Henry). Owen and Mifflin St Jeor equations were derived from the data of overweight and obese participants and hence have been suggested to better predict RMR in overweight and obese individuals [4].

Three equations developed in Asian populations from India, China and Japan were included in this study (Table 1). It was thought that Indian equations provide closer values to RMR measured in Sri Lankans because of the common ethnicity. However, Indian equations overestimated RMR in Sri Lankans by 202 ± 93 kcal/day indicating their unsuitability in predicting RMR in Sri Lankans adults. This inaccuracy may be attributed to the fact that the populations which these equations were developed were younger (18-30 years) than ours (19-60 years) and these equations were developed two and half decades ago in those whose energy intake and physical activity levels were likely to be different from our current population.

The equation of Liu was developed in a Chinese population and previous studies have suggested that Liu's equation is most

appropriate for predicting RMR in Chinese [29]. Liu's equation overestimated RMR values in Sri Lankans and can be considered not suitable for predicting RMR in Sri Lankans. The equation of Ganpule was developed in a Japanese population and validated by Miyake *et al.* [7] subsequently as being most suitable in the Japanese population. It was interesting to note that Ganpule equation showed the highest prediction accuracy compared to other equations in our population. However this equation overestimated RMR in Sri Lankans by a mean bias of 170 ± 102 kcal/day. We found that 65.4% of RMR values in Sri Lankans were overestimated by Ganpule equation even though comparatively it had the highest accuracy among other equations included in the present study.

Overestimation of RMR in Sri Lankans by existing prediction equations may be partly explained by ethnic variations, levels of physical activity, nutritional availability and consumption and biological and body composition variations. This work highlights the need for the development of a new equation for healthy Sri Lankans.

The strength of this study is that this is the first study that provides data on measured and predicted RMR in healthy Sri Lankans. One of the limitations is that this study did not obtain data for fat free mass (FFM) and fat mass (FM) and did not include the validation of equations that used FFM and FM as predictive variables. This exclusion was based on the fact that FFM and FM are not widely used field measures available for use in predicting RMR.

V. CONCLUSION

The findings of this study revealed that global prediction equations including equations developed in other Asian populations did not reach expected levels of accuracy for RMR prediction in Sri Lankans. Existing RMR prediction equation are not recommended for use to predict RMR in Sri Lankan populations and the need of developing a population specific prediction equation is emphasised.

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