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Effects of Sex and Weight on Fasting Blood Glucose in Mice Mus musculus, and Rats Rattus norvegicus

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Abstract: Fasting blood glucose is used to measure metabolic status and is important in the diagnosis and management of diabetes. Its study has continued to generate attention due to the increase in diabetes globally. Most of the reported studies have been on humans. This study, therefore, investigated the effects of sex and weights on fasting glucose levels in mice and rats. Forty-eight male and female albino rats weighing between 50-200g and twenty mice weighing between 16-28g were used for the study. The animals were acclimatized for two weeks. They were fasted overnight, and blood sample was collected from each animal for estimation of blood glucose. Their weights were measured, and blood glucose was determined by modified glucose oxidase method. The results of this study showed that male mice and rats have significantly heavier body weights and higher levels of fasting blood glucose compared with female rats and mice. The study shows that sex and weight affect fasting blood glucose levels in mice and rats. In conclusion, the finding of this study suggests that sex and weight should be considered for accurate assessment of metabolic status in mice and rats. This observation may also be relevant to the assessment of glucose metabolism in humans.

Keywords: Fasting Blood Glucose, Sex, Body Weight, Rats, Mice

1. Introduction

Sex differences in glucose homeostasis and diabetes have been reported [1, 3] Sex differences have been reported to cause variation in fasting levels of blood glucose [4, 5] Men have been reported to have higher levels of fasting blood glucose and are more insulin resistant [6, 7] while women have higher 2-h plasma glucose concentrations following oral glucose tolerance test (OGIT) [8]. Physiological differences in insulin sensitivity and beta cell function between males and females have been reported to contribute to sex differences in fasting glucose levels. Women are more insulin sensitive than men [7]. The female sex hormone estrogen has been reported to improve insulin sensitivity and suppress hepatic gluconeogenesis [9]. Differences in biology, culture, lifestyle, and environmental factors have been shown to contribute to sex differences and changes in glucose homeostasis [10, 11]. Genetic mechanisms played role in sex differences in the levels of fasting glucose and insulin [6, 12].

Sex differences in fasting blood glucose have been reported in nonhuman primates [13, 14]. There is higher prevalence of isolated impaired fasting glycemia in men than women [15, 16]. The studies by Chiu et al [17] showed an association between poor glucose regulation and weight gain in humans. Diabetes and impaired fasting glucose are diagnosed using fasting blood glucose level [18]. Positive correlation between fasting glucose, weight, and body fat has been reported in mice, nonhumans primates and humans [19].

There is little information regarding the effects of sex on levels of fasting blood glucose in rats and mice despite the use of these animals as preclinical animal models for metabolic study. Therefore, this study investigated the effects of sex and weight on fasting blood glucose levels in non-diabetic rats and mice.

2. Materials and Methods

Forty-eight rats (50-200g) and twenty mice (16-28g) were collected and housed two weeks for acclimatization. The animals were fed with animal laboratory chow and tap water was provided ad libitum. After two weeks of acclimatization and overnight fasting, blood sample was collected from the tail of each animal to estimate blood glucose level. Blood glucose was determined using modified glucose oxidase method [20]. The weight of each animal was also measured using electronic weighing scale.

3. Results

The data was analyzed using student t- test and results presented as mean + S. E. M.

P value < 0.05 was considered statistically significant for all analyses.

The results of the study are shown in tables 1-3 below:

Table 1. *Effects of sex and weight on fasting blood glucose levels in mice.*

Groups	Weights (g)	Fasting blood glucose (mg/dl)
Male mice (n=10)	*22.6±0.9	*108.7 ±7.4
Female mice (n=10)	17.2±0.3	91.6±7.4

The fasting blood glucose level in male mice was significantly higher than the female mice. Male body weights of mice were significantly heavier than the female mice *($p< 0.05$).

Table 2. *Effect of weight on fasting blood glucose levels in male and female rats.*

Weights	0-50g	51-100g	101-150g	151-200g
Fasting blood glucose (mg/dl) in male rats (n=6)	*106.8±2.3	*114.5 ± 7.8	*116.7 ± 2.9	*106.0 ±3.0
Fasting blood glucose (mg/dl) in female rats (n=6)	42.5±2.4	87.0 ± 3.3	69.2 ± 3.9	78.5 ± 3.3

The male rats have significantly higher levels of fasting blood glucose than female rats in different weight groups. *($p< 0.05$).

Table 3. *Effect of sex on fasting blood glucose level in rats.*

Groups	Fasting blood glucose (mg/dl)
Male rats (n=24)	* 111.0 ± 2.7
Female rats (n=24)	69.3 ± 9.6

Male rats have significantly higher fasting blood glucose levels than female rats. *($p< 0.05$).

4. Discussion

The study was undertaken to evaluate the effects of sex and body weights on fasting blood glucose levels in mice and rats. The results from the present study revealed that the levels of fasting blood glucose in both male rats and mice were higher compared with female rats and mice. The observed sex differences in fasting blood glucose levels of rats and mice in this study is consistent with previous studies in rats [12] and cynomolgus monkeys [13]. They reported that male rats and cynomolgus monkeys have higher levels of fasting blood glucose than the females. Male rats have been reported to have higher expression of hepatic gluconeogenic genes and higher hepatic glucose output [12] while female rats have more and higher pancreatic islets, and higher insulin concentrations [21]. The lower levels of fasting blood glucose in the female mice and rats compared with the males may also be due to female sex hormone estrogen. Estrogen improves insulin sensitivity and suppresses hepatic gluconeogenesis [9]. It also has been reported that estrogens increase electrical activity and modulate insulin secretion [22] and decrease glucagon secretion by preventing low glucose-induced calcium oscillations in alpha cells of the pancreas [23]. However, the study by Yue et al [14] reported there was no statistical difference in the levels of fasting glucose between normal male and female cynomolgus monkeys. The findings of this study also agree with the study in tree shrews (*Tupaia belangeri chinensis*) which reported that the male tree shrews have significantly higher body weights and higher fasting blood glucose level compared with the female tree shrews [24].

Studies in humans have reported sex differences in fasting glucose levels [6, 7, 25]. In humans, men have higher fasting glucose level than women due to differences in insulin sensitivity and beta cell function. Women are more insulin sensitive, have higher beta cell function [7, 26] and have greater glucose uptake by the skeletal muscle than men [27]. Differences in genetic mechanisms between males and females may also contribute to the observed sex differences in fasting blood glucose levels. The genes coding glucose metabolism are sex dependent [5, 12]. However, the results of the present study contrast the findings of Khan [28] who did not observe sex difference in fasting glucose level of humans.

The results of this study also showed that male mice and rats have significantly heavier body weights compared with female mice and rats. This finding agrees with the studies in tree shrews [24] and mice [19] which reported that male tree shrews and male mice have significantly heavier body weights than the females. The study by Palliyaguru et al [19] reported positive correlation between fasting glucose, weight and body fat in mice, non-humans primates and humans. The findings of this study also support the use of mice and rats as animal models for study in metabolism. This is because fasting blood glucose and body weight are parts of metabolic measures used to diagnose impaired fasting glucose and diabetes [18]. The results of this study further confirmed our understanding of the effects of sex and weight on fasting blood glucose levels.

5. Conclusion

The study showed that sex and body weight affected levels of fasting blood glucose in rats *Rattus norvegicus* and mice *Mus musculus*. Thus, the finding of this study suggests that sex and weight should be considered for accurate assessment of metabolic status in mice and rats. This observation may also be relevant to the assessment of glucose metabolism in humans.

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