FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 9 No. 7, July, 2025, pp 137 – 141
DOI: https://doi.org/10.33003/fjs-2025-0906-3671

HIGH SALT DIET REDUCES OVARIAN, UTERINE WEIGHT, AND FERTILITY INDEX IN FEMALE WISTAR RATS

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ABSTRACT

Female reproductive health is highly sensitive to hormonal and environmental factors, and diet is a significant modifiable factor influencing reproductive outcomes. This study aimed to investigate the impact of high-salt diets on the weight and size of the uterus and ovaries in female albino Wistar rats. Forty-four (44) female albino Wistar rats weighing between 200 and 250 g were randomly assigned to four groups comprising 11 albino Wistar rats each. The designated control group was fed with a non-high salt diet ad libitum; the other groups were fed 2.5 %, 3.5 %, and 4.5 % NaCl diets, respectively. All albino Wistar rats in groups 2, 3, and 4 were fed the experimental diet for 6 weeks. The male albino Wistar rats were housed separately before mating and allowed access to rat chow and water. The study showed that a high salt diet resulted in a significant decrease in the weight of the ovaries, the weight of the uterus and the fertility index. These findings show the importance of dietary regulation in preserving reproductive function and mitigating the adverse effects of metabolic disturbances. Thus, a high salt diet could be detrimental to the female reproductive system.

Keywords: High salt diet, Uterine weight, Ovarian weight, Fertility index

INTRODUCTION

Female reproductive health is highly sensitive to hormonal and environmental factors, and diet is a significant modifiable factor influencing reproductive outcomes (Khaw *et al*., 2008; Li *et al*., 2019). The female reproductive system, including the uterus and ovaries, is influenced by a complex interplay of hormones, including estrogen, progesterone, and gonadotropins, which regulate growth, function, and development of these tissues. Recent studies have suggested that high sodium intake may perturb this hormonal balance, potentially altering reproductive organ morphology and function (Veassalle *et al*., 2015). While excessive salt consumption has been primarily associated with cardiovascular and renal diseases, its impact on reproductive organs remains less well understood. For instance, elevated sodium levels have been shown to disrupt the hypothalamic-pituitary-gonadal (HPG) axis, which could have implications for ovarian function and uterine health (Fitzgerald *et al*., 2020; Hu *et al*., 2021). Furthermore, there is some evidence suggesting that high salt intake can promote systemic inflammation, oxidative stress, and endothelial dysfunction, all of which could negatively affect reproductive tissues (Wang *et al*., 2017). The effects of high salt intake on female reproductive health have been less frequently studied, with most research focusing on broader cardiovascular and renal outcomes. Recent studies have indicated that excess salt may lead to alterations in ovarian morphology, including changes in follicular development and ovarian weight (Yang *et al*., 2018), and may affect uterine histology, potentially influencing factors such as endometrial thickness and cell proliferation (Cacere *et al*., 2021). However, there is a gap in the literature regarding the direct effects of high salt consumption on the overall size and weight of the uterus and ovaries, key indicators of reproductive organ health. The current study seeks to fill this gap by investigating the effects of a high-salt diet on the weight and size of the uterus and ovaries and fertility index in female albino Wistar rats. By employing a controlled experimental design and morphometric analysis of reproductive tissues, this study aimed to provide insights into how excessive sodium intake could alter the structure of the uterus and ovaries, and whether such changes are associated with disruptions in reproductive function. Understanding the effects of high salt intake on reproductive health is increasingly important in the context of modern dietary patterns, where salt consumption often exceeds recommended levels. Given the global rise in chronic diseases related to excessive salt consumption, including hypertension and metabolic disorders (He *et al*., 2013), this research could contribute valuable information regarding the broader implications of salt on female reproductive health and inform future dietary guidelines.

MATERIALS AND METHODS

Materials

Sodium Chloride

The Sodium chloride NaCl (Batch No MC2/24/04, Production date, 04/2024) was purchased from a commercial vendor at Gwagwalada market, Abuja, Nigeria. The sodium chloride purchased was weighed using a weighing balance (SJ-30KWP) manufactured by Ohaus Corporation, Pine Brook, NJ USA.

Ethical Approval

Ethical approval was obtained from the University of Abuja Ethics Committee on Animal Use with approval number: UAECAU/2025/007.

Preparation of sodium chloride diet

The 2.5 % NaCl diet used for this research was prepared as described by the method of Asiwe *et al*., 2021. For every 100 grams of rat feed, 2.5 grams of NaCl was mixed properly with 97.5 grams of the rat chow (Asiwe *et al*., 2021).

Background screening

A pre-screening was done to ensure that the experimental animals were healthy. The animals were screened for

conditions such as fever that could affect their behaviour. This was done by observing the animals for signs such as lethargy, piloerection, hunched posture, and reduced food intake (Teeling *et* al., 2007; Wenger, 2012).

Experimental animals

Forty-four (44) female albino Wistar rats and twenty-two (22) male albino Wistar rats weighing between 200 and 250 g were used for the study. Animals were obtained from the animal unit of the University of Nigeria, Nsukka, Enugu State, Nigeria. Animals were housed in cages at the animal house of the Department of Human Physiology, University of Abuja, Abuja, Nigeria. They were allowed to acclimatize to laboratory conditions for two weeks (temperature 24-28°C, relative humidity 60-70 % and 12 h light-dark cycle) and given access to food and water following the method of Klein and Bayne (2007) (Klein and Bayne, 2007).

Experimental design

Animal grouping

The female albino Wistar rats were randomly assigned to four groups comprising 11 albino Wistar rats each. The designated control group (G1) was fed *ad libitum* with a non-high-salt diet feed, while the other groups (G2-G4) were fed diets containing 2.5%, 3.5%, and 4.5% NaCl, respectively. A range between 2.5 % to 4.5 % salt diet regime was used for this research since it has been established that a 3.5 % salt diet regime caused significant changes in the normal functioning of experimental rats (Wube *et al*., 2008). All albino Wistar rats in groups 2, 3, and 4 were fed the experimental diet for 6 weeks according to the method of Li *et al* (2020). The male albino Wistar rats were housed separately before mating and allowed access to rat chow and water.

Method of administration

The experimental diet was fed to the albino Wistar rats using feeding troughs, and the albino Wistar rats were allowed free access to the experimental diet. During the study, behavioural changes were monitored at a weekly interval.

Evaluation of organ weight

After six weeks of administration of a salt diet, four animals per group were sacrificed. The ovaries and uterus were removed immediately after sacrifice, and the organs were measured using a digital scale (Scout Pro, Ohaus Corporation, USA).

Statistical Analysis

Results obtained were presented as mean ± standard error of the mean. Comparison between groups was done using One-way analysis of variance (ANOVA) from the Statistical Product and Service Solutions version 20.0 (SPSS). The level of significance was set at $P<0.05$.

RESULTS AND DISCUSSION

Ovarian Weight in Animals Exposed to a High Salt Diet

In Table 1, the weight of the left ovary in the groups given a 3.5 and 4.5 % high salt diet (HSD) was significantly reduced ($P< 0.05$) compared to the control group. Although there was a decrease observed in the group given 2.5 % HSD, it was not statistically significant. Compared to the group that was given 25% HSD, the left ovaries were significantly ($P< 0.05$) reduced in the groups given 3.5 and 4.5 % HSD. The weight of the right ovaries was significantly reduced in all the HSD-exposed groups compared to the control. In the group given HSD at 4.5%, the right ovarian weight was significantly lower ($P< 0.05$) compared to the HSD 2.5% group.

Table 1: Left and right ovarian weight in animals exposed to a high salt diet

	Control (g)	2.5 % HSD (g)	3.5 % HSD (g)	4.5 % HSD (g)
Left Ovary	0.17±0.01	0.11±0.00	0.09±0.00^{ab}	0.08±0.00^{ab}
Right Ovary	0.19±0.02	0.11±0.00^{a}	0.10±0.00^{a}	0.09±0.00^{ab}

Superscripts (a) and (b) = $P< 0.05$ compared to the control and 2.5 % HSD, respectively

Uterine weight in animals exposed to a high salt diet

Figure 1 shows the result of HSD on uterine weight in adult female rats. The uterine weight in all the HSD-treated groups was significantly ($P< 0.05$) decreased compared to the normal control group. In the HSD 3.5 and 4.5 % groups, the uterine weight was higher compared to the group that was given HSD at 2.5 %. This was, however, only significantly ($P< 0.05$) higher in the group given HSD 4.5 %.

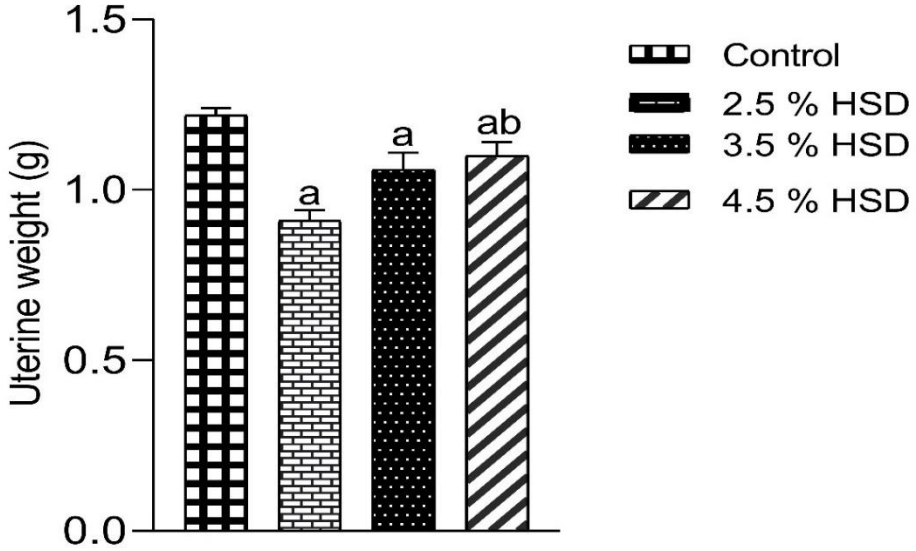

Figure 1: Uterine weight in adult female Wistar rats exposed to a high salt diet. HSD = high salt diet. Superscripts (a) and (b) = $P< 0.05$ compared to the control and 2.5 % HSD, respectively

Fertility Index in animals exposed to a high salt diet

In Figure 2, the percentage fertility in all the HSD-treated groups was significantly (P< 0.05) decreased compared to the normal control group. In the groups given HSD, the significant (P< 0.05) reduction in fertility index was in a dose-dependent fashion. Thus, the percentage fertility in the group given HSD at 4.5 % was significantly reduced (P< 0.05) compared to the groups given HSD at 2.5 and 3.5 %.

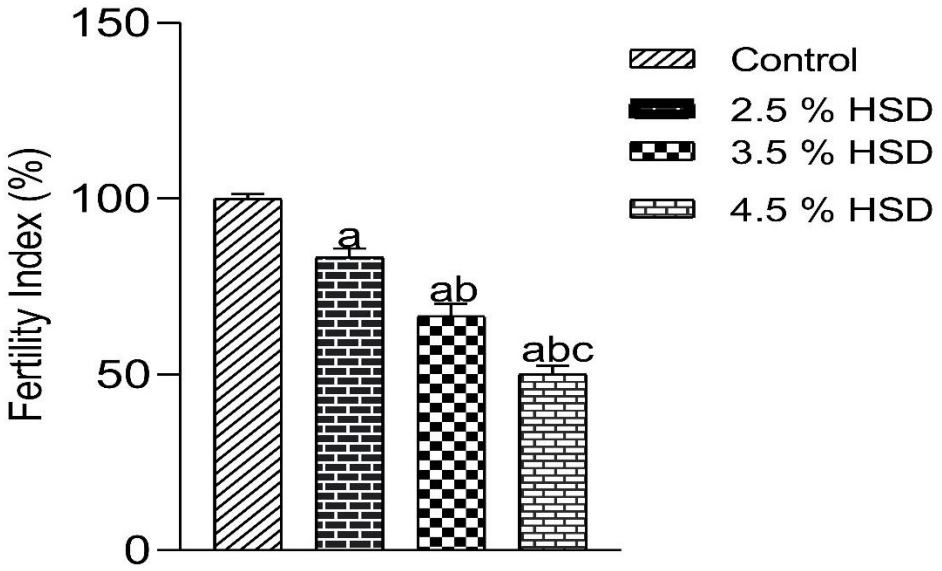

Figure 2: The percentage fertility index in adult female Wistar rats exposed to a high salt diet. HSD = high salt diet. Superscripts (a) and (b) = P< 0.05 compared to the control and 2.5 % HSD, respectively

Discussion

Studies suggest that excessive salt consumption can lead to oxidative stress and hormonal imbalances, which may contribute to weight reduction in the ovaries. For instance, research on salt loading in ovariectomized rats indicates that high salt intake exacerbates metabolic disturbances, including changes in lipid and glucose metabolism (Saleh *et al*., 2020). These disruptions could influence ovarian tissue integrity and function (Hou *et al*., 2022). Additionally, studies on maternal high-salt diets highlight their role in altering mitochondrial function and redox balance, which may contribute to tissue degeneration (Wang *et al*., 2015).

Furthermore, literature on polycystic ovary syndrome (PCOS) suggests that dietary modifications, including salt intake regulation, play a role in managing ovarian health (Tian et al., 2024). While PCOS is characterized by ovarian enlargement, excessive salt consumption may contribute to metabolic stress, potentially leading to ovarian weight fluctuations (Chi *et al*., 2024; Muhammed *et al*., 2025). In the present study, the results showing significant reductions in ovarian weight at higher salt concentrations (3.5% and 4.5%) reinforce the notion that excessive sodium intake can negatively impact reproductive organs. The observed differences between left and right ovarian weights could be attributed to variations in vascular supply or localized effects of oxidative stress.

The results on uterine weight indicate that a high-sodium diet (HSD) has a significant impact on uterine weight in adult female rats. The observed decrease in uterine weight across all HSD-treated groups compared to the normal control suggests that excessive sodium intake may contribute to alterations in reproductive organ physiology. However, the trend within the HSD-treated groups, where uterine weight was higher in the 3.5% and 4.5% HSD groups compared to the 2.5% group, suggests a dose-dependent response, with the highest sodium concentration (4.5%) showing a statistically significant increase. This pattern may be linked to metabolic adaptations or compensatory mechanisms in response to varying sodium levels. Sodium plays a crucial role in fluid balance and endocrine regulation, and excessive intake could influence hormonal pathways affecting uterine tissue (Gałęska *et al*., 2022). Previous studies have explored the effects of dietary sodium on reproductive health, particularly with estrogenic activity and uterine morphology (Silvestris *et al*., 2019; Kudesia *et al*., 2021).

The results suggest that a high-sodium diet (HSD) has a significant impact on fertility in a dose-dependent manner. The observed reduction in fertility index across all HSD-treated groups compared to the normal control indicates that excessive sodium intake may negatively affect reproductive health. The dose-dependent trend, where the highest sodium concentration (4.5%) led to the most significant decrease in fertility, suggests that increasing sodium intake exacerbates reproductive dysfunction.

This decline in fertility could be linked to metabolic stress, hormonal imbalances, or oxidative damage induced by excessive sodium consumption. Previous studies have explored the effects of dietary sodium on reproductive health, particularly concerning endocrine disruption and oxidative stress (Abdelnour *et al*., 2020; Peivasteh-roudsari *et al*., 2023). Research on reproductive toxicity has shown that dietary factors, including sodium levels, can influence fertility outcomes by altering hormonal pathways and affecting gamete viability (Yao *et al*., 2023; Chhabra *et al*., 2025).

These findings highlight the importance of dietary sodium regulation in maintaining reproductive health. The observed negative effects of high sodium intake on ovarian weight, uterine physiology, and fertility suggest that reducing excessive salt consumption may be beneficial in preserving reproductive function. Further studies are necessary to elucidate the precise mechanisms driving these effects and to determine potential interventions that mitigate sodium-induced reproductive toxicity.

CONCLUSION

This study demonstrates that high-salt diets significantly reduce the weight of the uterus and ovaries and lower the

fertility index in female albino Wistar rats. These findings highlight the critical role of dietary salt intake in female reproductive health and underscore the need for dietary regulation to prevent potential reproductive impairments associated with excessive salt consumption.

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