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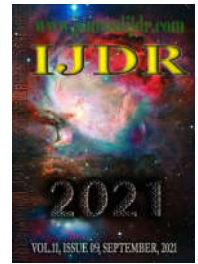
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## EVALUATION OF PLASMA PROTEIN LEVELS KLOTHO AND STRESS URINARY INCONTINENCE IN ELDERLY WOMEN AND THE IMPACT ON QUALITY OF LIFE

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### ABSTRACT

**Background:** Klotho is a protein that acts as a well-known anti-aging hormone, which serves as a suppressant of aging through a variety of mechanisms. The aging of skeletal muscle is concomitant with a decrease in the function of muscle stem cells, resulting in impaired regeneration. Stress urinary incontinence in women is still considered a challenge for medicine, impacting the quality of life of its carriers and its basic cause is tissue damage to muscle groups responsible for the support and functionality of the lower urinary tract. **Objective:** to study the potential functional role of Klotho protein in the tissue repair function of elderly patients with stress urinary incontinence was investigated, comparing its serum dosage to that of patients without the same pathology. In addition, in order to assess the impact caused by stress urinary incontinence in the lives of these women, a validated quality of life questionnaire was applied. **Results:** in assessing the quality of life measured by questionnaire of patients with urinary incontinence, it was observed, in relation to the severity of symptoms, that 62.5% of the patients reported that stress urinary incontinence interfered a lot in their lives. **Discussion and conclusion:** It was observed that patients with stress urinary incontinence had serum levels of klotho protein on average, higher compared to the group without urinary incontinence, translating possible biases and the need for long-term longitudinal studies.

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## INTRODUCTION

Since the beginning of the 1960s, Brazil's population has been aging rapidly. Advances in medicine and improvements in the general living conditions of the population have increased life expectancy at birth. Around the year 2000, life expectancy at birth reached 70.4 years and, according to projections, Brazil will continue to increase its population's average life expectancy, reaching, in 2050, the level of 81.3 years. Currently, 12.5% of the Brazilian population is 60 years old or more, which represents 23 million elderly people (MIRANDA; MENDES; SILVA, 2016; WORLD HEALTH ORGANIZATION, 2016). Human aging can bring countless challenges to care due to existing chronic pathologies. Among such challenges we can include Urinary Incontinence (UI), which can lead to problems for healthy aging and quality of life (HONÓRIO; DOS SANTOS, 2009). Urinary losses affect mainly women, of various age groups, but with a higher prevalence in elderly women, ranging from 26.2% to 37.9%, while in males it is 6.2% to 15.5% (SANTOS; SANTOS, 2010; ROSA *et al.*, 2014; TAMANINI *et al.*, 2009). The high prevalence in women may be due to physical-functional changes that occur in the aging process, such as, for example, menopause and menopause (SELBAC *et al.*, 2018). Thus, Stress Urinary Incontinence (SUI) has been a pathology that affects a significant number of postmenopausal women, imposing on them important situations of personal, family and social discomfort. SUI has multifactorial causes and has been associated with factors that facilitate its occurrence. However, there is still no available knowledge that reports a predictive value of its occurrence based on molecular markers (PEREIRA *et al.*, 2019; STOTHERS; FRIEDMAN, 2011).

Recently, genetic studies have identified a powerful aging suppressor gene, Klotho, which encodes a circulating membrane-bound hormone protein in mice and humans (KURO-O *et al.*, 1997; XIAO *et al.*, 2004). Klotho deficiency results in the appearance of numerous aging phenotypes, including decreased activity levels, gait disturbances and sarcopenia (CRASTO *et al.*, 2012; SEMBA *et al.*, 2012, 2016). The Klotho gene was identified and documented by Makoto Kuro-o *et al.* (1997). In Greek mythology, Clotho and his sisters Lahkesis and Atropos determine the fate of all human beings through the thread of life. Clotho is the goddess responsible for weaving the "thread" of life, Lahkesis determines the measure of each one's line and Atropos cuts the line indicating the end of life (KURO-O, 2009; PAVLATOU; REMALEY; GOLD, 2016). Klotho is expressed as a transmembrane protein from which the extracellular domain can be cleaved and released to function as a circulating hormone or expressed as a truncated form that is secreted or retained in the cytoplasm (KURO-O *et al.*, 1997; LI *et al.*, 2004; PACHECO; GONCALVES, 2014). Klotho has been studied primarily for its role in regulating renal function, where its expression level is higher and interest has focused on the impact of the progressive loss of Klotho expression during aging, which contributes to age-related changes in various organs, including kidney and skin. Klotho is also expressed at low levels in skeletal muscle, where its function is unknown (KURO-O, 2009; KURO-O *et al.*, 1997). There are two documented Klotho gene isoforms. The first provides the code for synthesizing a membrane protein while the second is identical to the first with the exception of a 50 base pair insert encoding a protein secreted into the circulation. The second isoform is predominant in all tissues when compared to the first isoform and, therefore, the main product of the Klotho gene is its protein secreted in blood, urine and cerebrospinal fluid (PACHECO; GONCALVES, 2014; PAVLATOU; REMALEY; GOLD, 2016). The relationship of circulating klotho with clinical phenotypes in human aging has not been studied due to the lack of a sensitive and reliable assay for measuring Klotho protein secreted into the blood. It is not known whether low plasma levels of Klotho are associated with low muscle strength in humans (PAVLATOU; REMALEY; GOLD, 2016; SAHU *et al.*, 2018). Aging is associated with impaired skeletal muscle regenerative capacity after an acute injury, resulting in declines in the capacity to produce force. The impaired regenerative response of aged muscle is characterized by a change in the functional repair of the myofiber after injury to

fibrotic deposition. This increase in fibrosis has been attributed to dysfunction of muscle stem cells (satellite) (MuSCs) (BRACK *et al.*, 2007). In response to muscle injury, MuSCs are activated from a resting state to repair damaged myofibers (SCHULTZ, 1989; SCHULTZ; GIBSON; CHAMPION, 1978). While activation of MuSCs in young muscle restores the original architecture of damaged myofibers, aging is associated with MuSC dysfunction, as evidenced by increased apoptosis, decreased proliferation, compromised autophagy and decreased resistance to stress (CONBOY *et al.*, 2003; GARCÍA-PRAT *et al.*, 2016; RYALL; SCHERTZER; LYNCH, 2008; ZERBA; KOMOROWSKI; FAULKNER, 1990). While young muscle is able to restore the original architecture of damaged myofibers, aged muscle exhibits markedly reduced regeneration. Expression of the "antiaging" protein, Klotho, is over-regulated in injured young muscles as a result of transient demethylation of the Klotho promoter. However, the epigenetic control of the Klotho promoter is lost with aging (SAHU *et al.*, 2018). Genetic inhibition of Klotho in vivo interrupts the progression of the muscle progenitor cell (MPC) lineage and impairs myofiber regeneration, revealing a critical role for Klotho in the regenerative cascade. Klotho gene silencing in young MPCs causes damage to mitochondrial DNA (mtDNA) and decreases cell bioenergetics (SAHU *et al.*, 2018). On the other hand, Klotho supplementation restores mtDNA integrity and bioenergetics of aged MPCs to young levels in vitro and improves the functional regeneration of aged muscle in vivo in a temporally dependent manner (SAHU *et al.*, 2018). These studies identify a role of Klotho in regulating the mitochondrial function of CPM and imply the decline of Klotho as a factor in compromising muscle regeneration with aging (SAHU *et al.*, 2018). Aging is accompanied by sarcopenia, defined as the loss of skeletal muscle mass and muscle strength (MORLEY *et al.*, 2001). Human beings can lose approximately 20-40% of skeletal muscle mass and strength from 20 to 80 years of age (CARMELI; COLEMAN; REZNICK, 2002; DOHERTY, 2003). Among the many underlying causes of sarcopenia are increased oxidative stress and inflammation, hormonal changes, aging anorexia as well as lack of physical activity (DOHERTY, 2003; SEMBA *et al.*, 2012). The Klotho protein may play a potential role in the pathogenesis of sarcopenia (SEMBA *et al.*, 2012). Klotho protein has not yet been evaluated in postmenopausal women from Distrito Federal, Brazil. Thus, this analysis will provide knowledge of the profile of SUI carriers or not, correlated with serum protein levels and quality of life. This may reflect on medical conduct, and on the future understanding of individualized care.

**Objetives:** Geral: To measure the serum levels of Klotho protein in postmenopausal patients who are or not with Stress Urinary Incontinence (SUI), and to assess the impact of SUI on the patients' quality of life. Specific: Know the epidemiological profile of postmenopausal patients with and without SUI; quantify circulating serum levels of Klotho protein by enzyme immunoassay; to compare the serum levels of Klotho protein between women with and without SUI.

## MATERIALS AND METHODS

**Study Design and Sample:** This is an observational, analytical cross-sectional study in postmenopausal women, elderly aged 60 years or over, attended at the Gynecology Outpatient Clinic of the Hospital Regional de Ceilândia – Distrito Federal, Brazil. **Sample:** At the time of medical care at the Gynecology Outpatient Clinic of the Hospital Regional de Ceilândia, the women were informed about the research and signed the Free and Informed Consent Term (TCLE). After agreement, blood collection, SUI diagnosis and quality of life were assessed through the patient's clinical history, physical examination and application of the King's Health Questionnaire. The selection of participants was made using the following criteria: Inclusion criteria: be female; be 60 years old or older; be able to understand, verbalize and answer the proposed questions. Non-Inclusion Criteria: having a neurogenic bladder and an overactive bladder; having undergone surgical treatment for UI correction; - having undergone clinical treatment for SUI; being a carrier of urinary fistulas; having a urinary

tract infection. The research participants were divided into two groups, with SUI and without SUI, comprising 24 and 23 participants, respectively. Blood collections were performed through venipuncture, in a closed vacuum system. After collection, the samples were sent to the Laboratory of Immunogerontology of the Catholic University of Brasília (UCB), where the serum Klotho protein concentration was analyzed using the Enzyme Immunosorbent Assay (ELISA) technique. -linked Immunosorbent Assay) using the specific kit produced by the company Uscn Life Science Inc., according to the manufactures instructions. All women who showed interest in participating in the research received detailed information about the research and signed the consent form (Appendix A). The TCLE, according to Resolution No. 466/2012 of the National Health Council (CNS) which provides for research with human beings, applied during the medical consultation at the Gynecology Outpatient Clinic of the Hospital Regional de Ceilândia. This work was approved by the Research Ethics Committee of the Faculty of Medicine of the University of São Paulo – FMUSP (CAAE: 42256214.4.3001.0065. Opinion number: 1,072,651) (Appendix B).

**Statistical analysis:** In order to assess the occurrence and strength of the association between Klotho's serum levels and the occurrence of SUI, our statistical analyzes began by obtaining Pearson's chi-square coefficients between the occurrence or not of SUI with the anthropometric categorical variables, clinical and biochemical to study the confounding effect in the main model. The chi-square test serves to quantitatively assess the relationship between the result of an experiment and the expected distribution for the phenomenon. That is, it tells us with how much certainty the observed values can be accepted as governed by the theory in question. In addition, biomarker concentrations were tested among individuals with or without SUI using the Mann-Whitney test. All analyzes were performed using the Statistical Package for Social Sciences SPSS for Windows (version 17.0), with an association being considered significant with  $p < 0.05$ .

## RESULTS

Descriptions and inferential statistics between patients with and without SUI, for age, weight, height, BMI, blood pressure, pregnancies, cesarean delivery, vaginal delivery and abortions.

**Table 1. Means and standard deviations of the variables of the SUI and non-SUI groups**

Variable	With SUI	Without SUI	p-value
Age (years)	67,3±6,2	65,7±4,8	0,417
Weight (kg)	67,6±11,7	71,6±15,7	0,282
Height (m)	1,5±0,1	1,5±0,1	0,773
BMI (kg/m <sup>2</sup> )	28,4±5	30,3±6,7	0,232
SBP (mmHg)	125,8±11	121,7±16,7	0,224
DBP (mmHg)	79,8±8,7	80±12,1	0,981
Pregnance (number)	4,7±2,7	3,7±2,5	0,327
Cesarean delivery	0,5±0,8	0,7±0,9	0,297
Vaginal delivery	3,5±2,3	2,8±2,5	0,354
Abortions	0,7±1,1	0,2±0,5	0,093

Source: Prepared by the author.

Regarding individuals with and without SUI, 18 patients (56.25%) had dystopia. In the group without SUI, 14 patients (43.75%) had dystopia. When considering the total number of dystopias, between SUI patients and non-carriers, 32 patients found this pathology, representing 68.09%. The same percentage was found in patients with SAH (Table 2). It can be seen that there are no statistically significant differences in the analyzed variables. Regarding individuals with and without SUI, 18 patients (56.25%) had dystopia. In the group without SUI, 14 patients (43.75%) had dystopia. When considering the total number of dystopias, between SUI patients and non-carriers, 32 patients found this pathology, representing 68.09%. The same percentage was found in patients with SAH (Table 2).

**Tabela 2. Fatores de riscopara IU Eem mulheres dos grupos com IUEsem IUE**

Variable	With SUI	%	Wiyhout SUI	%	Total	%
TRH	3	75	1	25	4	8,51
SAH	16	50	16	50	32	68,09
DM	3	25	9	75	12	25,53
Neoplasm	1	100	0	0	1	2,13
Sedentary	12	50	12	50	24	51,06
Active	12	52,17	11	47,83	23	48,94
Distopy	18	56,25	14	43,75	32	68,09
Smoking	8	53,33	7	46,67	15	31,91

Source: Prepared by the author.

In the items related to health assessment, 8 participants (33.33%) considered it bad. Only 2 individuals (8.33 %) consider it very good. Patients who considered it normal represent 29.17% of the sample (Table 3).

**Table 3. How do you rate your health today?**

Answer	Frequency	%
Very good	2	8,33
Good	5	20,83
Normal	7	29,17
Bad	8	33,33
Very bad	2	8,23
Total	24	100,00

Source: Prepared by the author

When analyzing the frequency of SUI and its impact on activities of daily living, it is noted that in 11 patients (45.83%) there is a significant predominance of the negative effect of the disease. Only 1 patient (4.17%) thinks he has no influence (Table 4).

**Table 4. How much do you think your bladder problem disrupts your life?**

Answer	Frequency	%
None	1	4,17
A little	5	20,83
More or less	7	29,17
A lot	11	45,83
Total	24	100,00

Source: Prepared by the authors

As for the impact of UI, 9 patients (60%) reported causing a lot of interference in homework and 6 patients (42.86%) reported that the impact of UI on work and activities outside the home, the negative effect was considered as "a little" (Table 5).

**Table 5. Impact of incontinency**

Answer	Frequency	%
On homework		
A little	4	26,67
More or less	2	13,33
A lot	9	60,00
Total	15	100,00
On your job?		
A little	6	42,86
More or less	5	35,71
A lot	3	21,43
Total	14	100,00

Source: Prepared by the authors.

Regarding physical limitations, 6 patients (31.58%) attribute to feeling uncomfortable in their activities. However, 7 patients (36.84) responded that they do not suffer any interference. In the item related to travel, the number of those who complain of interference is 8 patients (33.33%), equivalent to the number who do not complain of 8 (33.33%). In social participation, 9 patients (37.5%) reported not having any limitations and 15 individuals (62.5%) did not complain

about participating in family activities due to SUI. In personal relationships, SUI carriers had identical frequency and percentages in terms of sexual life. The 3 patients reported having no changes (27.27%). Identical frequencies and percentages answered: a lot and more or less. Regarding the relationship with the partner, 6 patients (54.55%) did not complain of interference and 20 patients (83.33%) reported that SUI does not interfere with their family life. In the evaluation of patients with UI regarding emotions, 8 individuals (33.33%) responded that they have no interference. However, 8 individuals (33.33%) reported that they feel the UI interference a lot. Regarding feeling anxious or nervous, 7 patients (29,17) reported that they feel the influence of UI a lot. When sleep or energy in UI patients was evaluated, 10 patients (41.67%) reported not being influenced and 16 patients (66.67%) said they did not feel worn out or tired. When the degree of severity of the vesical problem was evaluated in the item: if you use a protector to keep yourself dry, the variables sometimes, several times and always, represented 70.83% of the total.

15 patients (62.5%) complained that they lost a lot of urine in stress incontinence. Table 6 shows the summary of the Chi-square tests. From the p-value results, it is concluded that there are no significant relationships between the variables of having or not SUI. Table 7 shows the Klotho means with or without SUI and the p-value of the Mann-Whitney test. Based on the p-value, it can be concluded that there is a significant Klotho difference between having or not SUI, with Klotho being, on average, higher for those with SUI. The same is represented in Figure 1.

## DISCUSSION

Urinary incontinence is an important multifactorial health condition that can deteriorate women's quality of life. They feel ashamed and humiliated when talking about urinary incontinence, which is why many are reluctant to seek medical treatment (SINGH et al., 2013).

**Table 6. Summary of the Chi-square test between variables with or without SUI**

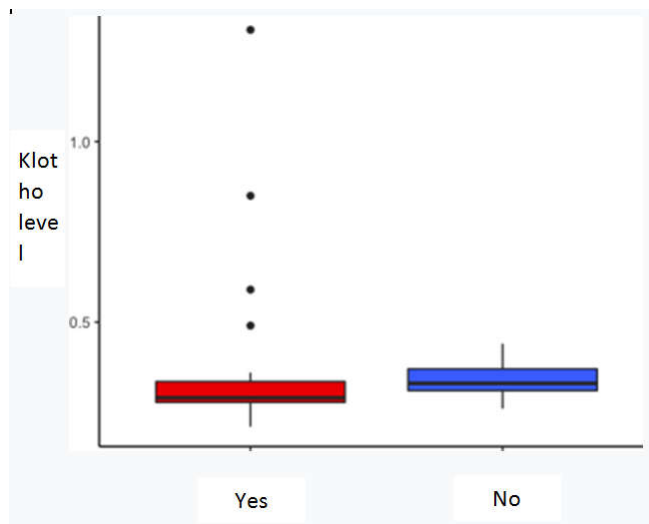
Variable	Chi-square	p-value
With HTR	0,229	0,632
SAH	0,000	1,000
DM	3,092	0,079
Neoplasm	0,000	1,000
Sedentary	0,000	1,000
Regular exercises	0,000	1,000
Dystopia	0,527	0,468
Smoking	0,000	1,000

Source: Prepared by the authors.

**Table 7. Means between serum Klotho levels and patients with and without SUI**

SUI	Average	Standart Deviation	Minimum	Q1	Median	Q3	Maximum	p-value
Yes	0,37	0,24	0,21	0,27	0,29	0,33	1,31	0,036*
No	0,33	0,04	0,26	0,31	0,33	0,37	0,44	

Source: Prepared by the authors.



Source: Prepared by the authors.

**Figure 1. Klotho dosage in patients with or without SUI**

And in the evaluation of fluid intake control, 8 patients (33.33%) reported that they always control. When the need to change underwear was analyzed because it gets wet and they are concerned about the odor of urine, 18 patients (43.33%) answered that they always change their clothes or worry about the smell of urine. Regarding the symptom severity scale, 8 patients (33.33%) responded that urinary frequency interferes a lot. In the nocturia item, 12 patients (50%) reported that they suffer a lot from the influence, and in the assessment of voiding urgency, 12 patients (50%) also reported suffering a lot. When the urge incontinence and stress incontinence were analyzed, 8 patients (33.33%) had a lot of urge incontinence and

The pathophysiology is in the epithelial changes in the urethral mucosa due to hormonal changes in women after menopause. After menopause, there is disruption of ovarian function that results in estrogen deficiency. Hormonal changes cause urinary incontinence due to changes in the urethral mucosa, loss of urethral closing pressure, bladder dysfunction, sphincter dysfunction or a combination of both (PEYRAT et al., 2008). The risk factors associated with urinary incontinence are: age, parity, type of delivery, previous hysterectomy, smoking habit, body mass index (BMI), diabetes mellitus, chronic cough and physical activities (DANFORTH et al., 2006; MARKLAND et al., 2011). To assess the quality of life of

patients, we chose to use the questionnaire validated for Portuguese (O King's Health Questionnaire) (FONSECA et al., 2005; TAMANINI et al., 2003). In this study, we evaluated the general health perception of patients with results reported that 11 patients (45.83%) reported that UI interferes a lot in their life and in 60% the impact of UI had a negative impact on quality of life. However, the physical/social limitation did not show important interferences. In the items personal relationships when evaluating the sexual life, 27.27% of the patients answered that the interference of the UI is too much and in the relationship with the partner 54.55% answered that the UI does not interfere. However, when considering emotions, 8 patients (33.33%) reported feeling depressed and 29.17% reported feeling anxious or nervous. When analyzing sleep/energy, 10 patients (41.67%) reported that UI does not affect their sleep and 16 patients (66.67%) responded that they do not feel tired.

As for the degree of severity of the bladder problem, 29.17% of the patients reported that they never use an intimate protector. However, 33.33% report that they always control the intake of liquids. An identical percentage of patients report that they always change their clothes because they get wet. Regarding the concern of getting urine odor, 41.67% report that they are always concerned. On the symptom severity scale, 50% of individuals complain of nocturia. Identical percentage presents voiding urgency. However, 15 patients (62.5%) have a lot of SUI. In our study, the descriptive and inferential statistics between patients with and without SUI, for age, weight, height, BMI, blood pressure, pregnancies, cesarean delivery, vaginal delivery and abortion, it is possible to see that there are no significant differences in the analyzed variables. However, it is known that menopause is a period characterized by metabolic, hormonal and clinical changes, caused by the progressive decline in ovarian activity and can also lead to psychosocial changes. It is characterized by high FSH levels and a decline in serum estradiol levels (HARLOW et al., 2012; VARELLA et al., 2016). Vasomotor, genitourinary and emotional symptoms appear at this stage. Among the genitourinary symptoms is the presence of lower urinary tract symptoms (LUTS). These are considered subjective indicators of changes perceived by women, classified as storage symptoms (polyuria, nocturia, urinary incontinence, urge urinary incontinence, mixed urinary incontinence, nocturnal enuresis, in addition to symptoms related to intercourse (dyspareunia and vaginal dryness) (DENYS et al., 2016; TERAUCHI et al., 2015). During menopause, the presence of LUTS is believed to be related to a decrease in urethral pressure, caused by a decline in estrogens, in addition to changes due to age itself, such as decreased blood circulation, insufficient stimulation of alpha-adrenergic receptors and atrophy of the vesical connective tissue (ROBINSON; TOOZS-HOBSON; CARDOZO, 2013).

Regarding overweight, it has been observed that the chance of developing UI in obese elderly women is 63% higher than in their normal weight peers (TAMANINI et al., 2009). In the present study, this association between UI and overweight was not significant ( $p=0.282$ ). The mean and standard deviation were: patients with SUI ( $67\pm 11.7$ ) and in patients without SUI ( $71.6\pm 15.7$ ). Our analyzes showed that, in relation to cesarean delivery, the mean and standard deviation were ( $0.5\pm 0.8$ ) and in those without SUI ( $0.7\pm 0.9$ ). In the group that underwent vaginal delivery, individuals with SUI had a mean and standard deviation of ( $3.5\pm 2.3$ ), while non-carriers had ( $2.8\pm 2.5$ ). Studies have shown that parity, delivery route or episiotomy are not risk factors for UI among the elderly population (SMITH et al., 2010; TAMANINI et al., 2009). Considering the percentage of patients with SUI and patients without SUI, the SAH variable showed that 50% of individuals have the disease. The consumption of medication for SAH is quite frequent in elderly women, especially diuretics (DA SILVA et al., 2012). However, the practice of physical exercise can contribute to reduce the consumption of diuretics in patients with SAH (MAZO; LOPES; BENEDETTI, 2009). In addition to the benefits to the course of the disease, the practice can also contribute to weight reduction, a factor that it is strongly related to the presence of arterial hypertension (BARROSO et al., 2008). Thus, physical exercise and the adoption of healthy habits, such as abstaining from fatty foods, reducing salt in

preparations, minimizing the use of alcohol and abandoning smoking, could significantly contribute to reduce the frequency of UI, especially among less active elderly women. Studies show that SUI has its incidence proportionally increased with aging, obesity, smoking, hypertension, diabetes, menopause and parity, especially in normal births. In addition, another important factor is gynecological surgeries, especially total hysterectomy, which by not preserving the uterine cervix, loses part of the pelvic floor support offered by the pericervical ring (DURU; JHA; LASHEN, 2012). It is estimated that more than half of patients with dystopias have UI during provocative maneuvers (SERATI et al., 2014). Our analyzes found 18 patients with dystopias (56.25%) with a diagnosis of SUI. In the group without SUI, 14 individuals (43.75%) did not report SUI. However, we did not find significance between the two groups ( $p=0.468$ ). In our study, the group with SUI, Klotho protein levels showed statistical significance ( $p=0.036$ ) compared to the group without SUI. That is, the group with SUI showed higher serum levels of Klotho protein (1.31ng/ml) versus (0.44ng/ml) in the group without SUI. Among the limitations of our study, we can mention the low number of patients recruited and the sample that involved only women aged over 60 years. In studies with patients of other age groups, new research may find other results. Therefore, broader studies can elucidate points that were obscured in our project.

## CONCLUSION

In the assessment of risk factors for stress urinary incontinence, when comparing the two groups with and without SUI, we found no significant differences in relation to hormone replacement, hypertension, diabetes mellitus, cancer, sedentary lifestyle, regular exercise, dystopia and smoking. In assessing the quality of life of patients with SUI, the KHQ demonstrates in the item severity scale of symptoms that 62.5% of patients responded that stress urinary incontinence interferes a lot in their lives. When analyzing the Klotho protein levels, patients with stress urinary incontinence had higher serum levels, on average, compared to the group without urinary incontinence.

### Glossary of Abbreviations

Akt: protein kinase B  
 BF: Biofeedback  
 CNS: National Health Council  
 DM: Diabetes *mellitus*  
 ELISA: Enzyme-Linked Immunosorbent Assay  
 EMT: Epithelial-Mesenchymal Transition  
 ES: electrical stimulation  
 FGFFibroblast Growth Factor  
 FGFR:: Fibroblast Growth Factor Receptor  
 SAH: Systemic Arterial Hypertension  
 ICIQ-SF: International Consultation on Incontinence Questionnaire - Short Form  
 ICS: International Continence Society  
 IGF-1: Insulin-Like Growth Factor-1  
 MAOI: Monoamine Oxidase Inhibitors  
 BMI: Body mass index  
 WILL: Acute Renal Failure  
 CKD: Chronic Kidney Disease  
 UI: Urinary incontinence  
 CUI: Continuous Urinary Incontinence  
 SIU: Stress Urinary Incontinence  
 IUM: Mixed Urinary Incontinence  
 PUI: Padoxical Urinary Incontinence  
 IUU: Urgent Urinary Incontinence  
 KHQ: King's Health Questionnaire  
 MPC: Muscle Progenitor Cells  
 mtDNA: Mitochondrial Deoxyribonucleic Acid (Mitochondrial DNA)  
 MuSCs: Muscle Stem Cells  
 DBP: Diastolic Blood Pressure  
 PBP: Systolic Blood Pressure  
 PTH: Parathormone

STUI: Lower Urinary Tract Symptoms  
 SUI: Stress Urinary Incontinence  
 BT: Behavioral Therapy  
 ICF: Informed Consent Form  
 TGF: Transforming Growth Factor  
 TMAP: Pelvic Floor Muscle Training  
 HRT: Hormone Replacement Therapy  
 LUT: Lower Urinary Tract  
 UCB: Catholic university of Brasilia

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