

Comparison of Relaxin Hormone Levels and Pelvic Floor Muscle Strength in Menopausal Women With Stress Urinary Incontinence & Without Stress Urinary Incontinence

Perbandingan Kadar Hormon Relaksin dan Kekuatan Otot Dasar Panggul pada Perempuan Menopause dengan Inkontinensia Urin Tipe Stres dan Tanpa Inkontinensia Urin Tipe Stres

Abstract

Objective : to determine the difference in relaxin hormone levels and pelvic floor muscle strength in postmenopausal women with stress urinary incontinence and without stress urinary incontinence

Methods : an unpaired categorical comparative analytic study with a cross sectional approach. The research sample was postmenopausal women at the Educational Network Hospital of the Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University in the period January-June 2021 who met the inclusion and exclusion criteria and were willing to participate. The number of samples was 50 people selected based on the consecutive sampling technique. Data were analyzed by Mann Whitney test and regression analysis at a significance level of 5%.

Results: the average relaxin level in postmenopausal women with stress urinary incontinence was 510.04 ± 121.59 pg/mL. The average relaxin level in control menopausal women was 667.96 ± 97.69 pg/mL. There was a significant difference in the average relaxin levels in postmenopausal women between stress urinary incontinence and controls with a p value of 0.000. The average pelvic floor muscle strength in postmenopausal women with stress urinary incontinence was 13.56 ± 7.72 cmH₂O. The average pelvic floor muscle strength in control menopausal women was 24.18 ± 11.29 cmH₂O. There was a significant difference in the mean pelvic floor muscle strength in postmenopausal women between stress urinary incontinence and controls with a p value of 0.000.

Conclusion : There are differences in relaxin hormone levels and pelvic floor muscle strength between postmenopausal women with stress urinary incontinence and without stress urinary incontinence.

Keywords: stress urinary incontinence, pelvic floor muscle strength, menopause, relaxin

Abstrak

Tujuan: mengetahui perbedaan kadar hormon relaksin dan kekuatan otot dasar panggul pada perempuan menopause dengan inkontinensia urin tipe stres dan tidak dengan inkontinensia urin tipe stres.

Metode: penelitian analitik komparatif kategorik tidak berpasangan dengan pendekatan cross sectional. Sampel penelitian adalah perempuan menopause di Rumah Sakit Jejaring Pendidikan Departemen Obstetri dan Ginekologi Fakultas Kedokteran Universitas Hasanuddin pada periode Januari-Juni tahun 2021 yang memenuhi kriteria inklusi dan eksklusi serta bersedia mengikuti penelitian. Jumlah sampel sebesar 50 orang yang dipilih berdasarkan teknik consecutive sampling. Data dianalisis dengan uji Mann Whitney dan analisis regresi pada taraf signifikansi 5%.

Hasil : rata-rata kadar relaksin pada perempuan menopause dengan inkontinensia urin stres sebesar $510,04 \pm 121,59$ pg/mL. Rata-rata kadar relaksin pada perempuan menopause kontrol sebesar $667,96 \pm 97,69$ pg/mL. Ada perbedaan signifikan rata-rata kadar relaksin pada perempuan menopause antara inkontinensia urin stres dengan kontrol dengan nilai p 0,000. Rata-rata kekuatan otot dasar panggul pada perempuan menopause dengan inkontinensia urin stres sebesar $13,56 \pm 7,72$ cmH₂O. Rata-rata kekuatan otot dasar panggul pada perempuan menopause kontrol sebesar $24,18 \pm 11,29$ cmH₂O. Ada perbedaan signifikan rata-rata kekuatan otot dasar panggul pada perempuan menopause antara inkontinensia urin stres dengan kontrol dengan nilai p 0,000.

Kesimpulan : Terdapat perbedaan kadar hormon relaksin dan kekuatan otot dasar panggul pada perempuan menopause antara dengan inkontinensia urin tipe stres dan tidak dengan inkontinensia urin tipe stres.

Kata kunci: inkontinensia urin stres, kekuatan otot dasar panggul, menopause, relaksin

INTRODUCTION

Urinary incontinence is a social problem and a person's quality of life. According to the International Continence Society, urinary incontinence is defined as the involuntary leakage of urine. Urinary incontinence has a major impact on the quality of life, the patient's own health status, causing impaired social relationships, psychological distress from embarrassment and frustration, hospitalization for skin damage and urinary tract infections, and sleep disorders.¹⁻²

The global prevalence of urinary incontinence ranges from 9.9% to 36.1%, and is twice as high in women as in men. In women, the prevalence was 24.9% experiencing stress urinary incontinence, 10.5% experiencing urgency urinary incontinence, and 5% experiencing mixed urinary incontinence. In Indonesia, the overall prevalence of urinary incontinence is 13% and increases with age. Urinary incontinence occurs in women twice as often as in men. This condition occurs in about 20-30% of young women, 30-40% of middle age and up to 50% of older women.²⁻⁴

Stress urinary incontinence is influenced by various factors including demographic characteristics (eg, age), lifestyle habits (eg, smoking), and initial medical conditions (eg, depression), as well as factors related to pregnancy and childbirth, urinary incontinence previous urinary tract infections, constipation, mode of delivery at the last delivery, previous urinary tract infections, body mass index during pregnancy, and menopause.⁵⁻⁷

Menopause was stated as a risk factor for stress urinary incontinence. This condition is associated with hormonal changes during menopause. Stated by Trutnovsky et al. that the symptoms and disorders of stress-type urinary incontinence are significantly associated with menopause age.[6] Alperin et al. stated that during menopause there is a decrease in endogenous estrogen levels which can cause pelvic floor disorders.^{6,8}

The mechanism of stress urinary incontinence in postmenopausal women is due to hormonal changes. During menopause, there is a decrease in levels of endogenous estrogen or estradiol (E₂). The level of estradiol (E₂) has a strong positive relationship with the level of circulating relaxin so that a decrease in E₂ can reduce relaxin levels. Low levels of estrogen and relaxin reduce the total collagen content and the ratio of specific collagen isoforms which can have an impact on decreasing the biomechanical properties of the pelvic connective tissue causing pelvic floor muscle dysfunction. The occurrence of pelvic floor muscle dysfunction causes stress urinary incontinence. Decreased levels of collagen can reduce the integrity of the pelvic connective tissue which causes pelvic floor muscle dysfunction.⁸⁻⁹

Ardiansyah et al. conducted a study with the aim of determining relaxin hormone levels in premenopausal and postmenopausal women with and without pelvic organ prolapse. The results indicated that the mean serum relaxin levels were not significantly different in women with pelvic organ prolapse and women with non-pelvic organ prolapse in menopause or in premenopause. Tendean detects urinary incontinence at postmenopausal age. The results showed that as many as 92% complained of urinary incontinence. Meanwhile, studies of differences in relaxin levels and pelvic floor muscle strength between postmenopausal women with stress urinary incontinence and without stress urinary incontinence have not been conducted before. Relaxin hormone levels and pelvic floor muscle strength are potential markers in predicting the occurrence of stress urinary incontinence in postmenopausal women. Therefore, researchers are interested in conducting a study that examines the comparison of relaxin hormone levels and pelvic floor muscles in postmenopausal women with and without stress urinary incontinence.¹⁰⁻¹¹

METHODS

This research is an unpaired categorical comparative analytic study with a cross sectional approach. The sample was postmenopausal women at the Educational Network Hospital of the Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University in January-June 2021 who met the inclusion and exclusion criteria and were willing to participate in the study. The number of samples was 50 people selected based on the consecutive sampling technique. The inclusion criteria of the study were postmenopausal women, diagnosed with stress urinary incontinence from history taking, physical examination, laboratory and results of The Questionnaire for Urinary Incontinence

Diagnosis (QUID) questionnaire, and willing to be included in the study by signing an informed consent. Exclusion criteria for the study were women who used hormone replacement therapy, menopausal women who experienced depression, women who used drugs such as anti-diuretics, antihypertensives and anxiolytics, and with symptoms of urinary incontinence due to other reasons. Data were analyzed by Mann Whitney test and regression analysis at a significance level of 5%.

RESULT

There are 50 research subjects, including 25 postmenopausal women with stress urinary incontinence and 25 menopausal women without stress urinary incontinence.

Table 1. Comparison of study subject characteristics between stress urinary incontinence and controls

Variable	stress urinary incontinence		Controls		Total		p€	
	n	%	n	%	n	%		
Age(56,12 ± 7,12)								
< 55 Years old	15	60,0%	10	40,0%	25	50,0%	0,314	
55 - 65 Years old	7	28,0%	12	48,0%	19	38,0%		
> 65 Years old	3	12,0%	3	12,0%	6	12,0%		
Occupation								
Unemployed/housewife	21	84,0%	17	68,0%	38	76,0%	0,321	
Employed	4	16,0%	8	32,0%	12	24,0%		
Education								
Primary education	17	68,0%	11	44,0%	28	56,0%	0,122	
Middle	7	28,0%	9	36,0%	16	32,0%		
Higher Education	1	4,0%	5	20,0%	6	12,0%		
BMI(23,44 ± 2,99)								
Normal	15	60,0%	16	64,0%	31	62,0%	0,274	
Overweight	8	32,0%	5	20,0%	13	26,0%		
Obesity	2	8,0%	4	16,0%	6	12,0%		
Duration of Menopause								
< 5 years	15	60,0%	15	60,0%	30	60,0%	0,904	
5 - 10 years	4	16,0%	5	20,0%	9	18,0%		
> 10 years	6	24,0%	5	20,0%	11	22,0%		
Parity								
Nulliparas	and						0,934	
primiparas		1	4,0	1	4,0	2		4,0%
Multipara		20	80,0	19	76,0	39		78,0%
Grande Multipara	4	16,0	5	20,0	9	18,0%		
Contraception								
Do not use	6	24,0	13	52,0	19	38,0%	0,130	
Hormonal	11	44,0	9	36,0	20	40,0%		
Non hormonal	5	20,0	1	4,0	6	12,0%		
Combined	3	12,0	2	8,0	5	10,0%		

Description: €Chi-square test; *significant at a significance value of 0.05; ** significant at a significance value of 0.001.

The subjects of this study had an average age of 56.12 years old. In menopausal women with stress urinary incontinence, most of them were less than 55 years old (60%), unemployed or

housewives (84.0%), Primary education (68.0%), normal nutritional status (60.0%), menopause less than 5 years (60.0%), multipara (80.0%) and using hormonal contraception (44.0%). The comparison of the characteristics of the study subjects between postmenopausal women with stress urinary incontinence and controls showed that there was no significant difference between the two based on age, occupation, education, Body Mass Index (BMI), duration of menopause, and contraceptive use (Table 1).

The average relaxin level in postmenopausal women with stress urinary incontinence was 510.04 ± 121.59 pg/mL. The average relaxin level in control menopausal women was 667.96 ± 97.69 pg/mL. These results suggested that postmenopausal women with stress urinary incontinence had lower relaxin levels than controls (Figure 1). The results of the comparison test of the average relaxin levels of postmenopausal women between stress urinary incontinence and controls resulted in a p value of 0.000 ($p < 0.05$). These results indicate that there is a significant difference in the average relaxin levels in postmenopausal women between stress urinary incontinence and controls (Table 2).

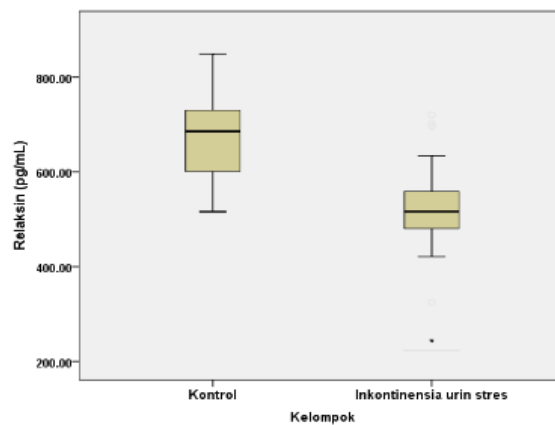


Figure 1. Comparison of the average value of relaxin levels in menopausal women between stress urinary incontinence and controls

Table 2. Comparison of the average relaxin levels of postmenopausal women between stress urinary incontinence and controls

Category	n	Relaxin (pg/mL)			p [£]
		Min	Max	Mean ± SD	
Stress Urinary Incontinence	25	233	720	510,04 ± 121,59	0,000**
Controls	25	516	849	667,96 ± 97,69	

Description: Mann Whitney test; *significant at a significance value of 0.05; ** significant at a significance value of 0.001.

Table 3. Comparison of the average value of pelvic floor muscle strength in menopausal women between stress urinary incontinence and controls

Category	n	Pelvic floor muscle strength (cmH ₂ O)			p [£]
		Min	Max	Mean ± SD	
Stress Urinary Incontinence	25	4,20	36,23	13,56 ± 7,72	0,000**
Controls	25	10,93	62,00	24,18 ± 11,29	

Description: Mann Whitney test; *significant at a significance value of 0.05; ** significant at a significance value of 0.001.

The average pelvic floor muscle strength in postmenopausal women with stress urinary incontinence was 13.56 ± 7.72 cmH₂O. The average pelvic floor muscle strength in control menopausal women was 24.18 ± 11.29 cmH₂O. These results showed that postmenopausal women with stress urinary incontinence had lower pelvic floor muscle strength than controls (Figure 2). The results of the comparison test of the average pelvic floor muscle strength of postmenopausal women between stress urinary incontinence and controls resulted in a p value of 0.000 (< 0.001). These results indicate that there is a significant difference in the mean pelvic floor muscle strength in postmenopausal women between stress urinary incontinence and controls (Table 3).

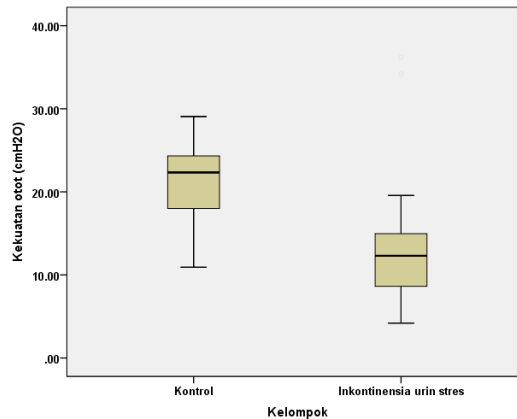


Figure 2. Comparison of the average value of pelvic floor muscle strength in menopausal women between stress urinary incontinence and controls

Table 4. The Effect of Relaxin Hormones and Muscle Values on Stress Urinary Incontinence

Variable	Odds ratio	95% CI	p ^y
Relaxin Hormones	0,952	0,907 - 0,999	0,045*
Pelvic floor muscle strength	0,862	0,730 - 1,017	0,079

Description: Regression test; *significant at a significance value of 0.05; ** significant at a significance value of 0.001.

Table 4 shows that the odds ratio for the relaxin hormone variable is 0.952. These results indicate that respondents with low relaxin hormone have a 0.952 times less chance of stress urinary incontinence than respondents with high relaxin hormone. The distribution value of the confidence interval of the odds ratio is from 0.907 to 0.999. The p-value obtained for the partial test on the relaxin hormone variable is 0.045, which is smaller than 0.05, indicating that the relaxin hormone has a significant effect on stress urinary incontinence. In addition, the test results on the muscle value show the results of the odds ratio value on the muscle value variable of 0.862. These results indicate that respondents with low muscle scores have 0.862 times less chance of stress urinary incontinence than respondents with high muscle scores. The distribution value of the confidence interval of the odds ratio is from 0.730 to 1.017. The p-value results obtained for the partial test on the muscle value variable of 0.079 which is greater than 0.05 indicates that the muscle value variable has no significant effect on stress urinary incontinence.

DISCUSSION

Association between relaxin levels and stress urinary incontinence in postmenopausal women

We found the average relaxin level in postmenopausal women with stress urinary incontinence was (510.04 ± 121.59) pg/mL and the average relaxin level in postmenopausal women without stress urinary incontinence was (667.96 ± 97.069) pg/mL and statistically significant ($p < 0.05$). The results in this study were higher than in the study conducted by Yam-na et al. where the relaxin level was (226.2 ± 178.8) pg/mL for postmenopausal women with pelvic organ prolapse and (108.4 ± 98.7) pg/ml for postmenopausal women without pelvic organ prolapse. Relaxin levels are associated with pelvic organ prolapse in postmenopausal women. Research of Ardiansyah et al. also reported the results that the relaxin levels in menopausal women with pelvic organ prolapse were lower than in menopausal women without pelvic organ prolapse, but the average relaxin levels of the two did not have a significant difference.^{10,12}

Normal levels of the hormone relaxin during the menstrual cycle are 420-480 pg/ml. Relaxin levels in postmenopausal women were reported as 172.0 pg/mL and 587.5 pg/mL for nonmenopausal women. Studies of stress urinary incontinence relaxin levels in postmenopausal women have not been studied before. A study of stress urinary incontinence relaxin levels was conducted on pregnant women where it was reported that the average relaxin level in women with 36 weeks of gestation who experienced stress urinary incontinence was 829 pg/mL. The average relaxin level was lower than the average relaxin level in women at 36 weeks gestation without stress urinary incontinence of 936 pg/mL.^{12,13}

The lower relaxin levels in menopausal women with stress urinary incontinence compared to non-stress urinary incontinence can be explained by the following mechanism. During menopause, there is a decrease in levels of endogenous estrogen or estradiol (E2). The level of estradiol (E2) has a strong positive relationship with the level of circulating relaxin so that a decrease in E2 can reduce relaxin levels. Low levels of estrogen and relaxin reduce fibroblast activation in producing TGF- β 1 which can have an impact on decreasing collagen synthesis, causing pelvic floor muscle dysfunction. Low TGF- β 1 expression is closely related to the occurrence of retrograde venous degeneration of the pelvic supporting structures. Low levels of estrogen and relaxin in menopause have also been shown to reduce the total collagen content and the ratio of specific collagen isoforms which can have an impact on decreasing the biomechanical properties of the pelvic connective tissue. Estrogen and relaxin can maintain the integrity of the pelvic connective tissue that affects the pelvic floor muscles. Low levels of estrogen and relaxin can reduce the integrity of the pelvic connective tissue which causes pelvic floor muscle dysfunction. The occurrence of pelvic floor muscle dysfunction causes stress urinary incontinence.^{8, 9, 14, 15}

Low levels of relaxin in postmenopausal women can reduce collagen levels and cause bladder neck hypermobility and intrinsic sphincter deficiency, causing pelvic floor muscle dysfunction which in turn causes stress urinary incontinence.¹⁶

Different results explained by Chen that there is an increase in relaxin levels in women with stress urinary incontinence. Stress urinary incontinence in women results from the degradation of collagen and elastin in the extracellular matrix of pelvic tissue, both of which give the pelvic floor the ability to recoil after physical stress. In women with stress urinary incontinence, there is an increase in relaxin concentration which causes a decrease in inhibition by -1 antitrypsin or an increase in elastase activity so that elastolytic activity increases in fibroblasts. Similar results were described by Ardiansyah et al. that relaxin is responsible for the elasticity of the reproductive organs, including cervical thinning, uterine contractility, intrapelvic ligament elongation, and may affect collagen turnover. One of its activities is to interact with estrogen. An increase in serum relaxin affects the elasticity and elongation of the tissue and can lead to a decrease in the type I:III collagen ratio, resulting in tissue weakening.^{10,17}

Type I collagen fibrils have a rigid structure that provides resilience and mechanical strength to tendons, whereas Type III collagen fibrils are thinner than type I fibrils and are present in high

concentrations in skin, blood vessels and other tissues with a large proportion of elastic fibers. Collagen III is another fibrillar collagen that has always been associated with type I collagen. The increase in serum relaxin decreases the ratio of collagen type I:III, meaning that the type I collagen which provides the strength effect is reduced and the collagen III which provides the elastic effect is increased. As a result, the overall strength of the network decreases.¹⁸

In this study, there were differences in relaxin levels between postmenopausal women with stress urinary incontinence and without stress urinary incontinence based on parity. Increased parity is a strong risk factor for the development of pelvic organ prolapse. Previous pregnancies, even without vaginal delivery, can cause urinary incontinence. In general, the strength and function of the endopelvic connective tissue is influenced by sex hormones including relaxin.¹⁹

Association between pelvic floor muscle strength and stress urinary incontinence in postmenopausal women

The results showed that the average pelvic floor muscle strength in postmenopausal women with stress urinary incontinence was (13.56 ± 7.72) cmH₂O. The average pelvic floor muscle strength in postmenopausal women without stress urinary incontinence was (24.18 ± 11.29) cmH₂O. The results of pelvic floor muscle strength in this study were higher than in Ismail and Ibrahim's study which obtained pelvic floor muscle strength of 7 cmH₂O in postmenopausal women with urinary incontinence. Chevalier, Fernandez-Lao and Cuesta-Vargas (2014) reported a cut off of pelvic floor muscle strength where cut off = 6 cmH₂O was in the very weak category, cut off = 8 cmH₂O was in the weak category and cut off = 10 cmH₂O was in the strong category. Thus, the results of pelvic floor muscle strength in this study, both in postmenopausal women with stress urinary incontinence and non-stress urinary incontinence, were included in the strong category.²⁰

The results are in line with the research from Baracho et al. that low pelvic floor muscle strength is the strongest predictor of stress urinary incontinence, physical therapy can be carried out to increase pelvic floor muscle strength to more than 35.5 cmH₂O in the prevention of stress urinary incontinence. The association between pelvic floor muscle strength and stress urinary incontinence was also described in the study from Price, Dawood and Jackson that pelvic floor muscle exercise helps to heal women with stress urinary incontinence. According to its function, pelvic floor muscle training aims to increase muscle strength and muscle tone to maintain or improve pelvic support and urinary sphincter closure system. Nygaard et al. adds that the bladder neck receives support from strong, tight pelvic floor muscles, which restricts downward movement and prevents stress urinary incontinence.²²⁻²⁵

The pelvic floor muscles play a very important role in maintaining continence function and supporting pelvic organs. Ho, Bhatia and Bhasin describe the anabolic effect of androgens on muscle and the mechanism by which testosterone regulates body composition with particular emphasis on the anabolic effect of androgens on the muscles of the pelvic floor and lower urinary tract in postmenopausal women. Androgens have a direct anabolic effect on skeletal muscle. Testosterone increases lean body mass and reduces fat mass. The action of testosterone on muscle involves a variety of mechanisms, including its effects on inducing protein synthesis, recruiting satellite cells, and modulating pluripotent mesenchymal cells in myogenic lineages. Other muscles of the pelvic floor and lower urinary tract are sensitive to the anabolic effects of testosterone. Androgen receptors are also expressed in the pelvic floor and urinary tract. The anabolic effects of androgens can cause abnormalities of the female pelvic floor and lower urinary tract.^{26,27}

Association between relaxin levels and pelvic floor muscle strength in menopausal women

The results of the comparison test between relaxin levels and pelvic floor muscle strength showed that relaxin levels had a more significant effect than pelvic floor muscle strength in the occurrence of stress urinary incontinence. Ardiansyah et al. stated that the low strength of the pelvic floor muscles

in stress urinary continence is related to low levels of the hormone relaxin which when low serum relaxin levels cause changes in collagen formation and degradation and can weaken the pelvic floor support system, so that the pelvic system loses its supporting dysfunction. However, this study did not conduct a direct study of relaxin levels on the strength of the pelvic floor muscles but conducted a study with pelvic organ prolapse.¹⁰

In this study, relaxin levels were not associated with pelvic floor muscle strength. These results support a previous study in a randomized controlled trial in postmenopausal women that did not find an independent effect of hormone therapy on increasing general pelvic floor muscle strength, and a retrospective study exploring the effect of menopause and hormone therapy on urinary incontinence found that the use of hormone therapy was positively related. with symptoms of nocturia, urgency urinary incontinence, and low urethral pressure. Antônio et al. in his study stated that in postmenopausal women, pelvic floor muscle training increased pelvic floor muscle strength more in women who did not use hormone therapy than in women who used hormone therapy.^{28,29}

Measurements of relaxin levels and pelvic muscle strength have been widely studied, but only few studies have been carried out in postmenopausal women. In addition, a study of the relationship between relaxin levels and pelvic floor muscle strength in postmenopausal women has never been performed. This is the strength of this research. This study only studied the relationship between relaxin levels and pelvic floor muscle strength, with insignificant results, while stress urinary incontinence pathology can also be caused by other influences such as pelvic muscle prolapse which were not investigated in this study.

CONCLUSIONS

Relaxin levels and muscle strength were significantly associated with the incidence of stress urinary incontinence. Relaxin levels in postmenopausal women with stress urinary incontinence were lower than those without stress urinary incontinence. Pelvic floor muscle strength in postmenopausal women with stress urinary incontinence was lower than those without stress urinary incontinence. Statistically, relaxin hormone levels are more dominant in causing stress-type urinary incontinence in postmenopausal women than pelvic floor muscle strength.

The implication of this study is that relaxin hormone and pelvic muscle strength can be markers to determine the possibility of stress urinary incontinence in postmenopausal women, however, relaxin hormone levels can be a marker that is prioritized over pelvic floor muscle strength. Further research can assess relaxin levels and pelvic floor muscle strength in women of reproductive age and premenopausal to observe the pathophysiology of stress urinary incontinence, and conduct a retrospective cohort study to examine the long-term effects of the hormone relaxin on stress urinary incontinence.

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REKOMENDASI PERSETUJUAN ETIK

Nomor : 600/UN4.6.4.5.31/PP36/2020

Tanggal: 29 September 2020

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH20090475	No Sponsor Protokol	
Peneliti Utama	dr. M. Mirza Aditya Hakim	Sponsor	
Judul Peneliti	Perbandingan Kadar Hormon Relaksin dan Otot Dasar Panggul Pada Perempuan Menopause Dengan Inkontinensia Urin Tipe Stres dan Tanpa Inkontinensia Urin Tipe Stres		
No Versi Protokol	1	Tanggal Versi	10 September 2020
No Versi PSP	1	Tanggal Versi	10 September 2020
Tempat Penelitian	RSUP Dr.Wahidin Sudirohusodo dan RS Jejaring di Makassar		
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard Tanggal	Masa Berlaku 29 September 2020 sampai 29 September 2021	Frekuensi review lanjutan
Ketua Komisi Etik Penelitian Kesehatan FKUH	Nama Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)	Tanda tangan	
Sekretaris Komisi Etik Penelitian Kesehatan FKUH	Nama dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Laporan SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari protokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan