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Relationship between Plasma Fibronectin Levels and Stretch Marks

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ABSTRACT

Introduction: Stretch marks or striae distensae are linear atrophic scars that form in areas of skin damage as a result of skin stretching. Mast cell degranulation and activation of macrophages occur as well as changes in the components of the extracellular matrix, including fibronectin. Fibronectin as a dimeric glycoprotein and components contained in the extracellular matrix, functions as a regulator of cellular processes, to maintain tissue and functions in the process of wound healing in tissues. The aim of this study was to determine the relationship between plasma fibronectin levels and stretch marks
Methods: This study was an observational study with a cross-sectional design of 40 females with stretch marks and 40 controls. Each patient underwent history, dermatological examination, and blood sampling to assess plasma fibronectin levels by ELISA test. These data were analyzed statistically using the Chi square test.
Results: The mean plasma fibronectin level in stretch marks was 259.541±165.937 ng/ml. The highest age with stretch marks was 18–25 years 33 (82.5%) people. Most of them had a family history of stretch marks from their mother 20 (50%) people. The majority of stretch marks are located on gluteus regions by 10 people (25%). The result of this study showed that there was a relationship between plasma fibronectin levels causing a risk of 2.85 times for stretch marks (p = 0.041).
Conclusion: There is a relationship between plasma fibronectin levels and stretch marks.

Keywords

Stretch marks, Striae distensae, Striae atrophicans, Fibronectin, Extracellular matrix.

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INTRODUCTION

Stretch marks, also known as striae distensae, are linear atrophic scars that form in areas of skin damage as a result of stretching of the skin.[1,2] Stretch marks are a cosmetic problem and cause discomfort to patients.[3,4] The prevalence of stretch marks that occur during puberty (6 % to 86%) and obesity (43%).[5,6] Stretch marks occur twice as often in women compared to men.[6] The most common locations for stretch marks occur on the stomach, breasts, upper arms, buttocks, and thigh.[5] Research conducted by Sipahutar, Jusuf, and Putra found that the location of stretch marks was mostly in the axilla, abdominal, cruris, gluteus and mammary regions (19.3%), as well as in the femur and gluteus regions (15.8%).[7]

The pathogenesis of stretch marks is still not known, but there are several mechanisms that cause stretch marks, genetic factors, mechanical factors, and hormonal factors.[8] Stretch marks begins with stretching, regardless of how strong the stimulus is.[8,9] Consequences This stretching causes degranulation of mast cells and activation of macrophages seen in the reticular dermis, as well as elastolysis of the extracellular matrix causing abnormalities in elastic fibers, collagen fibrils and other extracellular matrix components.[10-12] The cross-linking between collagen fibers is more important than the amount of collagen that allows stretch marks

to occur in response to stretching.[9] The extracellular matrix is altered by stretch marks, and one of these modifications is fibronectin is a dimeric glycoprotein that is present in the extracellular matrix and is essential for sustaining tissue and the extracellular matrix's composition. It also serves as a regulator of cellular activities. There are two forms of fibronectin, plasma fibronectin and cellular fibronectin. Moretti et al. found that plasma fibronectin is an important source of cellular fibronectin, which is needed for homeostasis and tissue repair.[13,14] Fibronectin plays a role in the structural integrity of the extracellular matrix and is also involved in the process of wound healing and tissue remodeling.[13] Based on the explanation above, there is a hypothesis that fibronectin has a role in the pathogenesis of stretch marks, but it is still limited, so research is needed to determine the relationship between plasma fibronectin levels and stretch marks.

METHODS

This study is an analytic observational study with a cross sectional design involving 18-40 years old of 40 females with stretch marks and 40 controls at the Dermatology and Venereology polyclinic in Universitas Sumatera Utara, Medan. Every research subject who informed consent was included in this study. The exclusion criteria were pregnant, Cushing's syndrome, Marfan's syndrome, diabetes mellitus, hypertension, coronary heart disease, atherosclerosis, stroke, liver disease, keloid, hypertrophic scar, psoriasis, and scleroderma. The ethical license was granted by the Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara.

The data collected by researchers at the work location of patients who come to Dermatology and Venereology polyclinic in Universitas Sumatera Utara, Medan. Researchers is taking a careful history, clinical examination, and blood sample tests to check plasma fibronectin. Plasma fibronectin levels were measured by using Human Fibronectin Elisa Kit. The data collected were analyzed using Chi-square test to determine the relationship between plasma fibronectin levels with stretch marks which $p < 0.05$ was considered a significant result.

RESULTS

In this study, the subjects were divided into stretch marks and control groups (with no stretch marks). The characteristics of the subjects based on age were presented in Table 1. Most of the research subjects in the stretch marks group were 18–25 years old (82.5%), while most of the control group were 18–25 years old (85%). According to family history, the majority of the stretch marks group had a family history, from their mother was 20 people (50%) and most of the control group had no family history was 17 people (42.5%) (Table 1). Table 2 shows the characteristics of subjects based on location stretch marks. We observed that 10 (25%) subjects had their stretch marks on gluteus areas, while 7 (17.5%) subjects had it on the femoral and gluteus areas.

Table 1. Distribution of research subjects by age and family history

	Stretch marks patients		Control	
	n=40	%	n=40	%
Age (years)				
18–25	33	82.5	44	85
26–35	7	17.5	11	15
36–40	0	0	0	0
Family History				
Mother	20	50	20	50
Sibling	7	17.5	3	7.5
Mother and sibling	10	25	0	0
No family history	3	7.5	17	42.5

Subsequently, the plasma fibronectin level was quantified utilizing the enzyme-linked immunosorbent assay (ELISA). The ELISA assay revealed that the concentration of plasma fibronectin in the group with

stretch marks was greater than that in the control group (259.541±165.937 ng/ml vs. 181.207±144.311 ng/ml) (Table 3). Upon evaluating the impact of plasma fibronectin on stretch marks, we observed an odds ratio (OR) value at 2.85 (p = 0.041) subjects with elevated plasma fibronectin levels have a 2.85 times increased chance of developing stretch marks compared to individuals with lower levels of fibronectin (Table 4).

Table 2. Distribution of research subjects by location of stretch marks

Locations	Stretch marks patients	
	n	%
Femoralis	4	10
Gluteus	10	25
Femoralis and gluteus	7	17.5
Gluteus and poplitea	4	10
Femoralis, gluteus and poplitea	7	17.5
Axilla, femoralis, and gluteus	1	2.5
Abdomen, femoralis, and poplitea	1	2.5
Abdomen, femoralis and gluteus	1	2.5
Axilla, abdomen, femoralis, and gluteus	1	2.5
Abdomen, femoralis, gluteus, and poplitea	1	2.5
Axilla, abdomen, femoralis, gluteus, and poplitea	1	2.5
Mammae, axilla, femoralis, gluteus, and poplitea	1	2.5
Mammae, axilla, abdomen, femoralis, and poplitea	1	2.5
Total	40	100

Table 3. Average plasma fibronectin levels in study subjects

Group	Plasma fibronectin levels		
	n	*Mean*	SD
Stretch marks	40	259.541	165.937
Control	40	181.207	144.311

Table 4. Relationship between plasma fibronectin levels and stretch marks

Plasma fibronectin levels	Group			
	Stretch marks	Control	Odd	p value*
High	22 (55%)	12 (30%)	2.85	0.041
Low	18 (45%)	28 (70%)		
Total	40 (100%)	40 (100%)		

**Chi square*

DISCUSSION

This study found that most of the research subjects in the stretch marks group were 18–25 years old (82.5%), while most of the control group were 18–25 years old (85%). Research conducted by Amal et al. in Dermatology and Venereology Polyclinic, Universitas Sumatera Utara Hospital, the highest distribution of stretch marks was found in women aged 18–25 years, with a mean age of 21.9 years.[15] The same condition was found in a study by Kasielska-Trojan and Antoszewski of 80 female students at the University of Lodz, Poland, with the mean age of women with stretch marks was 23.9 years (SD ± 2.05 years).[16] This is also in accordance with research by Putra, Jusuf, and Aryunisari on 155 female students at the Faculty of Medicine, Universitas Sumatera Utara Hospital, Medan, showed that the highest age group who had stretch marks was 19 years old (62.5%).[17] This shows that the prevalence of stretch marks is highest in group 18–25 years old.

According to family history, this study found that the majority of the stretch marks group had a family history, from their mother was 20 people (50%). Research conducted by Amal et al. in Dermatology and Venereology Polyclinic, Universitas Sumatera Utara Hospital, it showed that the majority of the stretch marks group had a family history of stretch marks, 39 people (54.2%) compared to 33 people without a family history of stretch marks (45.8%).[15] Stretch marks are caused by a genetic component that may be determined by genome wide association analysis. According to Tung et al., this genetic component includes gene variants

that code for fibrillin-1 and fibrillin-2, two components of elastic microfibrils.[18] The control group had no family history was 17 people (42.5%) and had a family history from their mother was 20 people (50%). Research conducted by Cho et al. on 157 teenagers in Korea found that family history was only found in 18 subjects (11.5%), compared to 139 subjects (88.5%) who had no family history of stretch marks. According to this research, there are other factors such as environmental, hormonal and physical factors that play a role in the process of forming stretch marks.[19]

According to the location, we observed that 10 (25%) subjects had their stretch marks on gluteus areas, while 7 (17.5%) subjects had it on the femoral and gluteus areas. This is in line with research by Amal et al. the most common locations found in the femoral and gluteus in 34 people (47.2%).[15] Research by Sipahutar, Jusuf, and Putra on 202 women with stretch marks, the femoral and gluteus regions were the second most common location for stretch marks to be found in 32 people (15.8%).7 The most common locations for stretch marks occur on the stomach, breasts, upper arms, buttocks, and thigh.[5]

The mean plasma fibronectin in the stretch marks group from our study were 259.541±165.937 and 181.207±144.311 in the control group. Until now, there is no research on plasma fibronectin levels in stretch marks patients. Regarding wound healing, plasma fibronectin is one of the extracellular matrix components that is important for controlling cellular reactions. Several studies have shown that the extra domain A isoform of fibronectin is upregulated in several chronic skin conditions including hypertrophic scars, keloids, psoriasis and scleroderma.[20-23] In this study, all of these things were excluded in the research subjects.

In this study, there were 22 subjects (55%) with high plasma fibronectin levels in the stretch marks group and 18 people (45%) with low plasma fibronectin levels in the stretch marks group. Based on the Chi square test, there is a statistically significant relationship between plasma fibronectin levels and stretch marks. High plasma fibronectin levels causing a risk of 2.85 times for stretch marks ($p = 0.041$).

Plasma fibronectin is a cellular response. If tissue damage or inflammatory processes occur, fibronectin is synthesized to function in the wound healing process. Fibronectin synthesis and fibrogenesis are driven by two cytokines, TGF- β and growth factors.[13] According to research by Singh et al., fibronectin molecules need to form fibrils in order for extracellular matrix to be synthesized. Fibronectin matrix is subsequently placed in wounds, where it promotes the deposition of collagen, which improves the healing process.[24,25] In wound healing, there was an increase in both the mRNA and protein expression of fibronectin. The extracellular matrix is entirely composed of fibronectin. In the process of regeneration or wound healing, locally synthesized cellular fibronectin migrates into the clot to regenerate the wounded tissue, while a form of plasma fibronectin is incorporated into the fibrin clot to form a temporary fibrin-fibronectin matrix.[26] TGF-β and other cytokines are released during the inflammatory phase of the healing process. This function of TGF-β depends on the presence of fibronectin in the extracellular matrix. Therefore, the wound healing stage is when TGF-β expression increases, and this is also when fibroblast migration and proliferation occur. Plasma fibronectin directly stimulates TGF-β release, fibroblast migration and proliferation, and enhanced collagen synthesis. Stretch marks can result from the process of stretching the skin, which can set off an inflammatory reaction and promote plasma fibronectin production in order to repair wounds. As a result, there is a possibility that this increase in plasma fibronectin contributes to the development of stretch marks.[24-26]

CONCLUSION

Based on the analysis of the data obtained from this study can be concluded that there was a relationship between fibronectin plasma and stretch marks. High fibronectin plasma levels cause a 2.85 times risk of stretch marks.

DECLARATIONS

This study was conducted after obtaining ethical clearance from the Research Ethics Committee of the University of Sumatera Utara (No. 191/KEPK/USU/2023) and from the Prof. Chairuddin P Lubis Universitas Sumatera Utara Hospital Research Permit (No. 1244/UN5.4.1.1.3/KPM/2023).

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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