Postural alteration, low back pain, and trunk muscle resistance in university students

Alteração postural, dor lombar e a resistência dos músculos do tronco em jovens universitárias

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Abstract

Introduction: Low back pain, the most prevalent musculoskeletal disorder, is common in individuals with postural changes and has a high incidence in university students. Trunk muscle instability and weakness can contribute to the presence of low back pain. However, no research has investigated the relationship between low back pain in conjunction with postural changes and the resistance of the trunk stabilizing muscles. **Objective:** To analyze the correlation between postural alterations and muscular resistance of the trunk of women with and without low back pain. Methods: Forty university women were recruited and divided into a group with low back pain (n = 20; 20.85 ± 1.69 years) and a group without low back pain (n = 20; 20.05 ± 2.54 years). On the first day, the postural assessment was carried out by photogrammetry with Kinovea software. On the second day, the resistance tests of the trunk flexor and extensor muscles, lateral and ventral plank, bridge, and lumbar traction were performed through the traction dynamometer. Pearson's correlation test was applied to verify the relationship between the analyzed variables, Student's T test was used for comparison between groups, and a significance level of p < 0.05 was adopted. **Results:** There was no correlation between the variables related to postural changes and muscle resistance tests (p > 0.05). There was a difference between the groups only for the bridge exercise test (p = 0.04) and vertical alignment of the head, left lateral view (p = 0.041), and right lateral view (p = 0.034). Conclusion: This study did not show a direct and significant relationship between postural changes in young university students with and without complaints of low back pain and resistance of the trunk-stabilizing muscles.

Keywords: Muscle strength. Photogrammetry. Posture.

Resumo

Introdução: A lombalgia, transtorno músculoesquelético mais prevalente, é comum em indivíduos com alterações posturais, que são de alta incidência em universitários. Instabilidade e fraqueza dos músculos do tronco podem contribuir para a presença da dor lombar. Não encontrou-se, contudo, pesquisas que tenham investigado a relação da dor lombar em conjunto com as alterações posturais e a resistência dos músculos estabiestabilizadores do tronco. **Objetivo:** Analisar a correlação entre alterações posturais e resistência muscular do tronco de mulheres com e sem dor lombar. Métodos: Foram recrutadas 40 mulheres universitárias divididas em grupo com dor lombar (n = 20; 20, 85 \pm 1,69 anos) e grupo sem dor lombar (n = 20; 20,05 \pm 2,54 anos). No primeiro dia, realizou-se a avaliação postural por fotogrametria com software Kinovea; no segundo dia, os testes de resistência dos músculos flexores e extensores de tronco, prancha lateral e ventral, ponte e tração lombar através do dinamômetro de tração. Aplicou-se o teste de correlação de Pearson para verificar a relação entre as variáveis analisadas, teste t de Student para comparação entre os grupos e adotou-se nível de significância de p < 0,05. Resultados: Não houve correlação entre as variáveis referentes às alterações posturais e testes de resistências musculares (p > 0,05); houve diferença entre os grupos apenas para o teste de exercício ponte (p = 0,04) e para o alinhamento vertical da cabeça vista lateral esquerda (p = 0,041) e vista lateral direita (p = 0,034). **Conclusão:** Este estudo não evidenciou relação direta e significativa entre as alterações posturais em jovens universitárias com e sem queixa de dor lombar com a resistência dos músculos estabilizadores do tronco.

Palavras-chave: Força muscular. Fotogrametria. Postura.

Introduction

Low back pain is considered the most prevalent musculoskeletal disorder.¹ Approximately 80% of people experience lower back pain at least once during their lifetime.² Although the main causes of low back pain are mechanopostural or degenerative,³ such as inflammatory or specific diseases, studies suggest an association between the disorder and the performance of the lumbar musculature, specifically in relation to the resistance of the trunk stabilizing muscles.^{4,5} The inability of these muscles to maintain prolonged levels of muscle contraction can have a negative effect on segment

stabilization.^{6,7} Instability of the posterior column delays nerve conduction, leading to reduced strength of the trunk muscles, which, in turn, can cause pain in the lumbar spine.⁸

In university students, studies point to a sedentary lifestyle,^{9,10} psychosocial changes,^{11,12} trauma¹³ and the presence of postural changes¹⁴⁻¹⁶ as factors associated with the onset of low back pain episodes. Postural alterations are a consequence of the relative misalignment of different segments of the body;^{17,18} however, body structures tend to seek homeostasis.¹⁹⁻²¹ Some authors have suggested that when identifying shortened or weak muscles, postural changes can be treated by strengthening and stretching the lumbar muscles.^{22,23}

Studies have reported a high incidence of postural alterations in university students. Santos et al.²⁴ found that 97% had scapular-pelvic unevenness, 85.7% had cervical hyperlordosis, 74.2% had trunk anteriorization, 65.7% had lumbar hyperlordosis, and 100% had a tendency for scoliosis. Falcão et al.¹⁵ identified a prevalence of 57.4% of cervical hyperkyphosis, 83.3% of head forward, 68.5% of hyperlordosis, and 66.6% of pelvis anteversion. Andrade et al.¹⁴ concluded that all participants experienced significant postural changes.

Postural changes in university students are associated with class routines, physical inactivity,²⁵ and sitting postures that are maintained for extended periods, which, as well as compensation and postural changes, generate an overload on the muscles, muscle fatigue and, consequently, compression of blood vessels and nerve endings, culminating in pain mainly in the spine.^{18,24,25}

Studies have identified, through photogrammetry, postural changes,^{14,24,25} related low back pain,¹⁴⁻¹⁶ as well as those that could suggest stabilization exercises for patients with low back pain.^{22,23} However, no studies have determined the relationship between low back pain and postural changes and resistance of the trunk-stabilizing muscles. Therefore, the objective of this study was to analyze whether there is a relationship between postural changes in young university students with and without complaints of low back pain and resistance of the trunk stabilizing muscles. Therefore, it is hypothesized that women with low back pain will show lower performance in the test of resistance of the stabilizing muscles of the spine and a higher incidence of postural alterations in relation to women without complaints of low back pain and that there will be a correlation between muscular resistance and postural alteration.

Methods

This is a cross-sectional, non-randomized, convenience sampling study. This project was approved by the Ethics Committee in Research on Human Beings of the Faculty of Philosophy and Sciences of Universidade Estadual Paulista (FFC-UNESP) under opinion no.3,640,442. The participants were informed of the procedures performed during the research and signed a free and informed consent form. All collections were performed at the Musculoskeletal Assessment Laboratory of the Center for Education and Health Studies (CEES) at FFC-UNESP.

Sample

The sample consisted of 40 female individuals, aged between 18 and 26 years, enrolled at FFC-UNESP, campus Marília, SP, recruited through direct contact with the researchers, and divided into two groups: with low back pain (LBP, n = 20) and without low back pain (NLBP, n = 20). The volunteers with LBP had at least two episodes of nonspecific low back pain in the last three months.²⁶ The sample size was determined using the G*Power program (effect = 0.85, power = 0.95, α error = 0.05, sample number for each group = 20, outcome variable = length of stay in the bridge exercise).

The eligibility criteria to participate in this study were: age between 18 and 30 years old, being a university student enrolled in an undergraduate course with a body mass index (BMI) up to 30 kg/m² and not having neurological or orthopedic disorders that would affect the tests, discrepancy between the lower limbs greater than two centimeters, ankylosing spondylitis, rheumatoid arthritis, herniated disc, tumor, infection, vertebral fracture, cauda equina syndrome, or use of anti-inflammatory or analgesic drugs.

Evaluation procedures

Assessments were performed individually by the same researcher on two consecutive days in 2021. On the first day, anamnesis and postural assessments were performed, and on the second day, muscle performance tests were performed. The evaluations were conducted at the Laboratory of Musculoskeletal Assessment (LAM) of UNESP.

Postural assessment

Postural assessments were performed using photogrammetry. The volunteers wore black tops and shorts, allowing a clear view of the contours and anatomical points. For the registration of photos in the anterior and sagittal frontal planes (right and left), participants were instructed to remain in an orthostatic position, with bare feet and hair tied, and to assume a comfortable and relaxed posture.

Images were obtained using a Nikon digital camera (COOLPIX P90) and analyzed using Kinovea software,²⁷ installed on a Lenovo notebook, i5-8265U, 8GB, 1TB, Windows 10, Ideapad S145. The participants were positioned 15 cm from the wall, on top of the marking made on the ground, and photographs were taken at a distance of 2.4 m, with the camera fixed on the tripod at a height of 1 m, to view the whole body.²⁸ The wall and floor were covered with black TNT for better visualization of the volunteer and standardization of the photographs. Styrofoam markers measuring 25 mm in diameter were cut in half and glued with double-sided tape to the following anatomical points bilaterally: ear tragus, acromion, anterior superior iliac spine, posterosuperior iliac spine, greater trochanter, head of fibula, center of patella, tibial tuberosity, and lateral malleolus.²⁹

Postural changes evaluated in the anterior frontal plane were head tilt to the right or left, shoulder tilt to the right or left, pelvic tilt, and right and left Q angles. In the right and left sagittal plane, the following were evaluated: anteriorization and posteriorization of the head, anterior and posterior trunk inclination, pelvic anteversion and retroversion, the presence of flexed knee and recurvatum, and dorsiflexion and plantar flexion, as suggested by Ribeiro et al.²⁹ Figure 1 shows how the postural changes selected in the Kinovea software were analyzed.

Muscle performance tests

Six tests were used to evaluate the resistance of the stabilizing muscles of the spine. Prior to evaluation, the volunteers were familiarized with the tests, the researcher explained and demonstrated the test, and the volunteer performed it at least once to ensure that the execution was correct.



Figure 1 - Analysis of anterior, right and left side views in the Kinovea software.

For data collection, each test was performed only once, in the order described below, under a standardized verbal stimulus, with a three-minute interval between each test to avoid possible muscle fatigue.

1) Bridge: In dorsal decubitus, arms along the body, knees flexed at 90° and aligned with the hip, and feet fixed on the stretcher. The volunteer raised the pelvis and contracted the glutes.²² The time (in seconds) was calculated using a digital stopwatch from the moment the pelvis was elevated until the participant was unable to remain in the position.

2) Ventral plank: In the prone position, the patient flexed her elbows and shoulders at 90° and raised her pelvis so that it was aligned with her trunk and head,²² keeping only her forearms supported in a neutral position of prone-supination and fingers and forefoot. The test was timed in seconds using a digital stopwatch and ended when the participant was unable to maintain the horizontal position.

3) Lateral plank: In lateral decubitus, the volunteer placed the ipsilateral elbow flexed at 90°, forearm in neutral position for prone-supination, and shoulder at approximately 90° abduction. The legs were extended in line with the trunk, with the foot contralateral to the decubitus position in front of the other. A freehand was placed on the opposite shoulder. The test time was

measured in seconds using a digital stopwatch from the moment the volunteer assumed the position of lateral elevation of the pelvis until the trunk and lower limb contralateral to the decubitus were aligned until the moment when she could not maintain the position.²²

4) Resistance test of the trunk extensors: The volunteer was positioned in the prone position on a stretcher, with the upper part of the body out of it and the anterosuperior iliac spine aligned with the stretcher. The lower part of the body was fixed to the stretcher using three bands positioned around the ankle joint, above the knee joint, and in the region below the buttocks.²² During the test, the patient kept her upper limbs crossed over her chest and hands resting on the contralateral shoulder. A bench was placed in front of the participant to support her body before the beginning and at the end of the test. The test time was measured in seconds using a digital stopwatch from the moment the patient assumed the horizontal position until the moment she could no longer maintain that position.³⁰

5) Flexion resistance test: The volunteer was instructed to sit and perform trunk flexion at 60° under the guidance of the researcher who used the universal goniometer as a form of measurement. The forearms remained crossed in front of the torso, with the hands supported anteriorly to the contralateral shoulders, hips in neutral positions, knees aligned and flexed at 90°, and feet fixed to the mat. The test time was calculated in seconds using a digital stopwatch, starting when the participant was positioned at 60° and ending when the patient's trunk was no longer in the correct angulation.²²

6) Traction dynamometer: To perform the muscular actions of lumbar traction, the evaluated person stood on the platform of the dynamometer, the knees were completely extended, the trunk was slightly flexed in front, and the head followed the extension of the trunk with the stare straight ahead. Both hands were separated by a distance equal to their bitrochanteric diameter.³¹ In this position, the volunteer applied the greatest possible muscular force to the muscles of the lumbar region, pulling the support bar up and leaving the lumbar spine erect. Therefore, the volunteer was advised to avoid leaning back or performing any additional movements with the legs and/or arms, such as bending the knees and/ or elbows.³¹ Each participant familiarized themselves with the test with an initial attempt. Each recorded data point represents the average of three measurements and was normalized by body mass [strength (N)/body mass (kg)].

Statistical analysis

Statistical analysis was performed using PASW Statistics software (SPSS, version 18.0°). After verifying the normality and homogeneity of the data using the Shapiro-Wilk test, Student T test was applied to compare the variables between the groups, and Pearson's correlation was used to verify the relationship of the analyzed variables. In all statistical tests, a significance level of p < 0.05 was adopted.

Table 1 - Sample characteristics

	NLBP (n = 20)	LBP (n = 20)	р
Age (years)	20.05 ± 2.54	20.85 ± 1.69	0.771
Mass (kg)	58.05 ± 9.76	58.79 ± 9.48	0.810
Height (cm)	162.60 ± 6.08	163.05 ± 4.83	1.000
BMI (kg/m²)	22.25 ± 2.85	22.02 ± 3.01	0.924

Note: NLBP = no low back pain group; LBP = low back pain group; BMI = body mass index. Mean values ± standard deviation.

Results

The characteristics of the samples are presented in Table 1. It can be observed that in relation to age, body mass, height, and BMI, the groups did not differ (p > 0.05).

Regarding the assessment of muscle performance, there was a significant difference between the groups only in the bridge (p = 0.004), and the LBP presented a time 35.36% shorter than that of the NLBP, as shown in Table 2.

For the postural changes analyzed, the only variables that showed a significant difference between the groups were the vertical alignment of the head, left lateral view (p = 0.041), and right lateral view (p = 0.034). The NLBP presented the degrees of vertical alignment head view left side with values 37% lower than that of the LBP and 30% lower in vertical alignment of the head view right side, as shown in Table 3. In the Pearson's correlation analysis, no significant correlation was found between the analyzed variables (p > 0.05), as shown in Table 4.

Table 2 - Time spent performing muscular resistance exercises in the groups without and with low back pain

Exercise	No low back pain group	Low back pain group	р
Bridge (sec)	251.00 ± 103.55	162.25 ± 78.71	0.004
Ventral plank (sec)	63.35 ± 35.09	50.40 ± 19.37	0.157
Left side plank (sec)	42.45 ± 18.48	36.05 ± 16.30	0.253
Right side plank (sec)	44.55 ± 22.23	36.40 ± 16.64	0.197
Trunk extensors resistance (sec)	101.90 ± 31.65	86.15 ± 42.10	0.189
Flexural strength (sec)	164.60 ± 104.28	135.50 ± 73.69	0.315
Traction dynamometer (N/kg)	1.21 ± 0.22	1.17 ± 0.29	0.614

Note: sec = seconds; N/kg: Newton/kilogram. Mean values ± standard deviation. Values in bold = statistical significance.

Discussion

The objective of this study was to identify whether there is a relationship between postural changes in young university students with and without complaints of low back pain and performance of the trunk stabilizing muscles. According to the results, the initial hypothesis of the study was refuted given that in most muscle tests there was no difference between the groups. Furthermore, no correlation was found between test results and postural changes. Sadler et al.³² reported that reduced transverse plane control of the hip due to gluteus medius weakness tends to increase femoral internal adduction, rotation, and knee valgus, causing anterior rotation of the ipsilateral pelvis, which alters the load on the lumbar spine and increases the risk of low back pain. In the present study, as no differences were found in performance in the resistance tests of the trunk stabilizer muscles between young people with and without low back pain, it may also justify the absence of significant differences in postural changes.

Postural changes (degrees)	NLBP	LBP	р	
Horizontal head alignment	- 0.30 ± 2.11	- 0.95 ± 3.22	0.520	
Horizontal alignment of the acromions	- 0.25 ± 2.00	- 0.85 ± 2.30	0.384	
Pelvic tilt	- 0.05 ± 2.68	- 0.90 ± 2.79	0.332	
Right Q angle	27.40 ± 10.59	26.90 ± 13.89	0.179	
Left Q angle	27.70 ± 9.13	29.35 ± 9.98	0.371	
Vertical head alignment - left side view	9.45 ± 9.26	15.00 ± 7.25	0.041	
Vertical trunk alignment - left side view	-2.60 ± 2.58	- 3.60 ± 2.82	0.249	
Horizontal alignment of the pelvis - left side view	-11.95 ± 5.32	- 14.55 ± 5.84	0.149	
Knee angle - left side view	0.80 ± 4.63	- 1.20 ± 4.63	0.180	
Ankle angle - left side view	2.20 ± 2.46	1.70 ± 2.58	0.534	
Vertical head alignment - right side view	12.20 ± 8.63	17.45 ± 6.30	0.034	
Right trunk vertical alignment - right side view	0.20 ± 2.89	- 0.05 ± 3.35	0.802	
Horizontal alignment of the pelvis - right side view	-15.45 ± 4.32	- 17.05 ± 5.43	0.309	
Knee angle - right side view	0.45 ± 3.43	- 1.80 ± 3.81	0.057	
Ankle angle - right side view	5.20 ± 2.17	4.10 ± 2.63	0.157	

Table 3 - Postural changes analyzed in the groups

Note: NLBP = no low back pain group; LBP = low back pain group. Mmean values ± standard deviation. Values in bold = statistical significance.

Jesus et al.,³³ awhen pooling studies that included hip strengthening exercises for the treatment of people with low back pain, concluded that hip strengthening exercises improved pain and disability in people with low back pain compared to interventions where strengthening the hip was not used, suggesting that the gluteal muscles provide pelvic stability in the frontal plane, which, in turn, provides a stable base for the lumbar spine (especially during unipedal support tasks), protecting the body from low back pain. However, the authors did not discriminate which glutes are more important for stability and protection against low back pain.

In the sample studied, the only muscle endurance test that showed a difference between LBP and NLBP was the "bridge," which presents greater demand for the gluteus maximus muscle.³⁴ Cooper et al.³⁵ rcarried out a study with 150 individuals with nonspecific chronic low back pain and 75 control individuals and concluded that the gluteus medius is weaker in people with low back pain.

Kim e Yim³⁶ investigated how core stability affects physical function and activity in patients with nonspecific low back pain and observed that strengthening the core muscles decreases pain intensity and improves quality of life.

The data of the present study, due to the lack of difference in performance in five tests of muscular

resistance related to the core between the LBP and NLBP and the difference in the test in which the performance depended preponderantly on the gluteus maximus, suggest that the resistance of the core muscles does not differ between young people with and without low back pain, with the gluteus maximus being stronger in young people who do not have low back pain, but without significant implications for postural changes.

Regarding the postural alterations evaluated in the present study, the only variable that presented a significant difference between the groups was vertical alignment of the head. Although previous studies have found a relationship between low back pain and postural changes,¹⁴⁻¹⁶ from the results of the present study, new searches were carried out looking for negative results of this relationship, and there was a scarcity in the quantity and quality of studies that prove that there is no relationship between low back pain and postural changes.

Ribeiro et al.³⁷ did not identify a correlation between the presence of low back pain, static posture, and flexibility, which corroborates the findings of this study. However, the study identified the need for more research in this area to confirm these results. Graup et al.³⁸ also found no relationship between low back pain and sagittal deviations in adolescents.

Postural changes (degrees)		Bridge (sec)	Ventral plank (sec)	Left side plank (sec)	Right side plank (sec)	Trunk extensors resistance (sec)	Bending resistance (sec)	Traction dynamometer (N/kg)
Horizontal head alignment	R	0.157	- 0.057	- 0.089	- 0.122	- 0.062	- 0.049	- 0.188
	р	0.335	0.725	0.583	0.452	0.704	0.765	0.246
Horizontal alignment of the acromions	R	0.015	0.056	0.038	- 0.046	0.069	0.159	- 0.051
	р	0.927	0.732	0.817	0.780	0.672	0.328	0.754
Pelvic tilt	R	- 0.075	0.144	0.013	- 0.032	- 0.074	- 0.284	- 0.287
	р	0.645	0.376	0.938	0.846	0.652	0.076	0.072
Right Q angle	R	- 0.066	- 0.191	- 0.180	- 0.099	- 0.100	0.106	- 0.158
	р	0.695	0.250	0.280	0.553	0.551	0.519	0.344
Left Q angle	R	- 0.087	0.035	- 0.218	- 0.182	- 0.213	- 0.083	- 0.158
	р	0.604	0.835	0.188	0.275	0.186	0.622	0.344
Vertical alignment of	R	- 0.062	0.177	0.153	0.184	- 0.116	0.046	- 0.170
the LSV head	р	0.702	0.275	0.345	0.257	0.477	0.780	0.294
Vertical alignment of	R	- 0.091	0.137	0.031	0.106	- 0.153	- 0.062	- 0.039
the LSV trunk	р	0.578	0.400	0.848	0.514	0.346	0.706	0.810
Horizontal alignment	R	- 0.136	- 0.223	- 0.209	- 0.151	- 0.013	0.130	0.084
of the pelvis LSV	р	0.403	0.166	0.195	0.354	0.937	0.426	0.608
Knee angle LSV	R	- 0.103	0.043	- 0.126	- 0.016	- 0.151	0.067	- 0.116
	р	0.526	0.791	0.438	0.920	0.354	0.681	0.477
LSV ankle angle	R	- 0.218	- 0.065	- 0.120	- 0.012	- 0.196	0.033	- 0.141
	р	0.177	0.688	0.462	0.939	0.225	0.841	0.386
Vertical alignment of the RSV head	R	0.029	0.090	0.060	0.090	- 0.198	- 0.126	- 0.245
	р	0.857	0.582	0.714	0.582	0.221	0.438	0.128
Vertical alignment	R	0.148	0.168	0.090	0.170	0.083	0.161	0.382
of the RSV trunk	р	0.363	0.299	0.580	0.294	0.610	0.320	0.015
Horizontal alignment	R	- 0.156	- 0.307	- 0.306	- 0.157	- 0.050	0.161	- 0.060
of the RSV pelvis	р	0.335	0.054	0.055	0.334	0.758	0.320	0.712
Knee angle RSV	R	- 0.018	- 0.078	- 0.129	0.016	- 0.059	0.211	- 0.137
	р	0.910	0.633	0.428	0.921	0.719	0.191	0.398
RSV ankle angle	R	- 0.121	- 0.013	- 0.121	- 0.074	- 0.050	0.234	- 0.066
	р	0.457	0.935	0.456	0.649	0.759	0.147	0.686

Table 4 - Correlation between length of stay in muscular resistance exercises and postural changes analyzed in the groups without and with low back pain

Note: LSV = left-side view; RSV = right-side view. R = correlation value; p = p-value of the statistical correlation test.

Shortz e Hass,³⁹ ain a sample of 352 patients with chronic low back pain, investigated pain-related factors with special emphasis on radiographic postural findings in the sagittal lumbosacral spine, and found no correlation between lumbar hyperlordosis and levels of pain. Pain in patients with chronic low back pain. Similarly, Jouibari et al.⁴⁰ also did not find differences in the curvature of cervical lordosis between patients with

nonspecific neck pain and healthy controls, reinforcing the non-mandatory postural changes in the presence of musculoskeletal pain, probably because they are of multifactorial origin.³⁸

The data obtained in the present study are important and contribute to greater scientific knowledge about low back pain and postural changes in young people. However, the eligibility criteria for the low back pain group can be considered a limitation. The occurrence of at least two episodes of nonspecific low back pain in the last three months seemed to be a broad criterion, in which many volunteers fit in even without identifying low back pain as something that impairs functional capacity, allowing them to remain in the tests for longer. The inclusion of questionnaires that assess the impact 2. Nava GTA, T

capacity, allowing them to remain in the tests for longer. The inclusion of questionnaires that assess the impact of low back pain on daily activities, such as the Roland Morris or Oswestry Disability Index, could contribute to a better characterization of the groups, as well as establish the chronicity of low back pain as a criterion. Another suggestion for future research on the same topic is to include more specific strength and endurance tests for the gluteus medius muscle, given its importance in pelvic stability.³² Despite continuous investigations and the development of new interventions, musculoskeletal pain in the spine remains a clinical challenge because of its multifactorial nature and high incidence.³⁸

Conclusion

The data of the present study, under the methodological conditions used, did not show the existence of a direct and significant relationship between postural changes in young university students with and without complaints of low back pain and resistance of the trunk stabilizing muscles. These findings suggest that other musculoskeletal conditions may be involved in differentiating between women with and without low back pain.

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Authors' contributions

RAF and DHS were responsible for writing the manuscript and, together with MTN, for designing, analyzing, and interpreting the data. All authors approved the final version of the manuscript.

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