

Research Article





Causes of low back pain (LBP) in women without pregnancy, in relation to different age groups during the reproductive period, are primarily treated as musculoskeletal disorders: a retrospective study

Abstract

Introduction: Low back pain (LBP) is a musculoskeletal disorder of several causes that can mess up the spine. It is characterized by pain, stiffness or muscle tension and is usually localized in the lumber region. – During their working years, people frequently experience low back pain. Approximately 84% of adults experience LBP once or more during their lifetime. In Bangladesh, wt. related prevalence of LBP is 18.5% and age group 18-34 years prevalence are 10.5% and >55 years 27.8%, average 19.2%, which is more in women 27.2% than men.

Pain in the soft tissue of the back is extremely common among adults and often affects individuals during their working years. LBP in women, is strongly linked to hormonal and reproductive factors, the work environment and lifestyle. Females frequently experience lower abdominal and back pain at reproductive age, usually due to PMS, PMDD, dysmenorrhea, endometriosis, pregnancy, menopause, muscle spasms, arthritis, UTI, PID, HTN, DM, obesity, multiple C/S tracts and lower abdominal operations, all of which cause RAD, osteoporosis, vertebral and intervertebral disc diseases (PLID, herniation, slipping etc.). The $L_{_{\rm 4}}$ and $L_{_{\rm 5}}$ neural arches are involved in the transmission of a considerable load. Therefore, the joints between the articular facets of L₄ and L_s,- are sites of LBP. Low back pain (LBP) was diagnosed by history and clinical examination according to the Pain Scale. To determine the cause of HELLP syndrome/causes by routine investigations and sometimes abdominal ultrasonography (USG), magnetic resonance imaging (MRI) is needed. Treatment of LBP depends on the cause. When a definite lesion is not found, the patient should be informed and reassured about the treatment of LBP.

Purpose/Objective of the study: To identify the causes of LBP and prevalence of LBP in women of reproductive age excluding pregnant individuals and establish referral guidelines.

Methodology: This was a retrospective (observational) cross sectional study jointly conducted by Orthopedics and Gynecology Expertise in the North-East region, named the Sylhet Division of Bangladesh. Female patients were considered to be of reproductive age for the last three (3) years (2020 - 2022) at the Z&J fellows medical institution. The data were collected from the medical records of computer databases with preset questionnaires and written informed consent. The 1st part of the questionnaire consisted of questions about the causes of LBP, and the 2nd part consisted of LBP-related questionnaires. Patients were selected by the inclusion and exclusion criteria. The data were analyzed with SPSS 25.0 statistical software, MS Word and Excel version 2010. Descriptive statistics were analyzed, i.e. - frequency, central tendency and dispersion, i.e. range, standard deviation and variance. Tests of "proportions" and "significance" were performed via sample t-tests and ANOVA. Statistical data analysis was used to evaluate the correlation of LBP incidence and intensity (%) with age, BMI, disease status, marital status, obstetric history, working history and posture of reproductive-age women.

Summary: LBP has multiple causes. In retrospective studies, there is no way to predict the prevalence of causes rather, the prevalence of causes can be determined before patients are affected. In our study, we explored the causes of LBP in women according to age, BMI, local and systemic diseases, marital history, obstetric history, working history and posture. The prevalence of LBP was greater in the 41-50 years age group (34.7%) and in the 20-30 years age group (34.2%). Moreover, overweight and obesity are associated with LBP. Overall 5.3% and 12.8% of the participants were overweight and obese, respectively, and were aged >20-30 years with LBP. Patient age, BMI, disease status, marital status, obstetric history and working history had no effect on any

Volume 16 Issue 3 - 2024

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Received: April 25, 2024 | Published: May 13, 2024

of the patients, but some patients had LBP; overweight, obesity, age group and working posture had direct effects on LBP incidence (p>0.05). LBP is more common in women- than in men and may be due to household activities and a greater frequency of visceral pain during menstruation, pregnancy and labor.

Conclusion: Low back pain (LBP) can occur in multiple physical conditions in women of reproductive age except during pregnancy and can disrupt the back tissues of the lumbosacral region. Women are more susceptible to LBP because of menstrual and obstetric factors. A diagnosis was made by obtaining a meticulous detailed medical history, performing a physical examination and performing proper investigations. The causal parameters revealed that LBP had no effect on any of the patients, but women of reproductive age may suffer from LBP due to differences in cause.

Message of the article

LBP in women of reproductive age except pregnancy is multifactorial effect of back tissues, especially lumber region. LBP has a major socioeconomic impact on patients and leads to disability. Proper evaluations are mandatory to identify the causes of the underlying pathology of pain generators before starting treatment. Patients were referred to an opposite medical person when they met the relevant guidelines; i) the findings were suggestive of serious medical and psychological issues; ii) activity limitations and impairments in body functions were reported; and iii) symptoms were not resolved with interventions.

Keywords: low back pain (lbp), women of reproductive age, lbp in women without pregnancy, retrospective, cross-sectional study, overweight, obesity





Abbreviations: BMI, body mass index; CD, cesarean delivery; CM, centimeter; CVD, cardiovascular disease; DM, diabetes; HLS, healthy lifestyle; H/O, history of; IVD, intervertebral disc; kg, kilogram; LA, lower abdomen; LAOs, lower abdominal operations; LBP, low back pain; NVD, normal vaginal delivery; OA, osteoarthritis; OB, obesity; OW, overweight; PMS, premenstrual syndrome; PMDD, premenstrual dysphoric disorder; PID, pelvic inflammatory disease; PLID, prolapse lumber intervertebral disc; RAD, rectus abdominis diastasis; STD, sexually transmitted disease; SUI, stress urinary incontinence; UI, urinary incontinence; UTI, urinary tract infection; Wt., weight

Introduction

Low back pain (LBP) is a musculoskeletal disorder that can mess up the spine. It is characterized by pain, stiffness or muscle tension, and is usually localized in the lumber region. During their working years, people frequently experience low back pain. Approximately 84% of adults experience LBP once or more during their lifetime. Pain in the soft tissue of the back is extremely common among adults and often affects individuals during their working years. LBP in women is strongly linked to hormonal and reproductive factors, the work environment and lifestyle. 3

It is a major sickness that causes individuals severe consequences for health care resources. ^{3,6–8} In 2020, approximately 10% of the population worldwide suffered from LBP. A study of the Global Burden of Disease (GBD) in 2021 showed that LBP became under resourced and overburdened in social and health care systems in Asia and Africa. Chronic LBP has a greater effect on the socioeconomic condition of populations. The incidence of chronic LBP is approximately 23%, and 11-12% of the population becomes disabled due to LBP.²

LBP is associated with personal, social and financial compulsion worldwide. The National Health Care Services costs for LBP were approximately 5 billion pounds (£) in the UK annually and 134 billion US\$ in 2016 in the U.S. but the United States, National Institute of Health (NIH) was able to decrease the costs of LBP by 69 million US\$ in 2023. LBP and other musculoskeletal diseases are the leading causes of disability, but there is no specific mention of these disorders in the context of WHO non-communicable diseases (NCDs) or the NCD 2030 Countdown.⁶ In Bangladesh, 18.5% and 19.4% of weightrelated LBP outbreaks are associated with age. LBP is more common in females than in males.² The WHO and NIAMS (NIH) classify LBP according to the duration of low back pain (LBP) as follows: i) acute back pain that occurs suddenly and lasts a few days to a few weeks; ii) subacute back pain that occurs suddenly or over time and lasts 4-12 weeks; and iii) chronic back pain that occurs quickly or slowly and lasts more than 12 weeks and continues daily. 1,9-11 Pain is probably dull, constant to sudden, and sharp and may radiate to the lower limb/ limbs. 10 In France, 90% of patients recover from pain within two (2) weeks.8 Another study reported that approximately 80% of cases of back pain lasted less than one week.12

There are various causes of LBP, including gynecological, vascular, neurological, psychological, spine (spondylogenic) or disc pathology as well as traumatic, but the cause may be undiagnosed and enclosed by the term "mechanical or postural back pain". These may be mechanical or structural abnormalities of the spine, inflammatory conditions and/or other medical conditions. Pathology can include the spine, disc, muscle, ligament or tendon on the back or nerve compression.^{3,11}

LBP during pregnancy may be defined as recurrent or continuous pain for more than a week from the lumber spine as a result of different nonspecific causes. This type of pain is typically due to weight gain and psychological and prolonged postures, such as – sitting, standing or repeated lifting. During pregnancy, LBP was associated with hypermobility, high BMI, absence of menstruation and previous H/O back pain. Younger pregnant women more frequently experience back pain with multiple pregnancies and severe physical or psychological work. A total of 80.8% of the pregnant women felt pain in the lumber region, and 49.1% of the pain originated in the sacroiliac joints.

Females frequently experience lower abdominal pain with back pain at reproductive age, usually due to menstrual cycle related factors (e.g., PMS, PMDD and dysmenorrhea); endometriosis; pregnancy; menopause; muscle spasms; arthritis; UTI; PID; HTN; DM; obesity; multiple C/S; and lower abdominal operations causing RAD; uterine prolapse usually occurs after 50 years of age; intrauterine contraceptive device use; and osteoporosis, vertebra and intervertebral disc disease (PLID, herniation, slipping etc.). 15,16

Women are more affected than men by low back pain (LBP),^{3,5} and strong thinking has shown that this difference is due to the female reproductive system. The female musculature and ligament support are weaker than those of men; furthermore, pelvic girdle muscles and ligaments undergo strain during pregnancy and labor and suboptimally regain their normal state after delivery.3 The incidence of LBP is greater in married women than in unmarried women. More vaginal deliveries and live births are associated with LBP.17 A greater number of abortions is also directly associated with back pain. 18 The incidence of LBP in women associated with pregnancy, gynecological factors and other diseases is -66%, 35% and 24%, respectively, of women suffer during pregnancy, and 51% experience LBP during menstruation.^{1,18} Women who underwent cesarean delivery (CD) had a 4.5 fold greater risk of rectus abdominis diastasis (RAD). 24.6% incidence of LBP in RAD.4 Obesity, pregnancy, number of live births, CD, RAD, abortion, infection, inflammation, HTN, DM, spondylogenic and discogenic factors, trauma, working environment, posture and psychological effects are risk factors for LBP in women during their reproductive age.

Low back pain (LBP) was diagnosed by history and clinical examination according to the Pain Scale. To determine the cause of HELLP syndrome/causes by routine blood and urine tests and sometimes abdominal ultrasonography (USG), magnetic resonance imaging (MRI) is needed.^{3,5} Treatment of LBP depends on the cause. When a definite lesion is not found, the patient should be informed and reassured about the treatment of LBP.³

Materials and methods

This was a retrospective (observational) cross sectional study jointly conducted by Orthopedics and Gynecology Expertise in the North-East region, named the Sylhet Division of Bangladesh; the study included female patients of reproductive age without pregnancy in the last three (03) years (2020 - 2022) at the Z&J fellows' medical institution. The total population in this area is 9.5 million. The main occupations in tea gardens, were agriculture and day labor. The data were collected from the medical records of computer databases with preset questionnaires and written informed consent.

The 1st part of the questionnaire consisted of: height, weight, BMI, medical history (HTN, DM, UTI, PID, RAD, arthritis, PLID, renal stone, and psychological), marital history (marital status, marital age and marriage duration), obstetrical history (no. of pregnancies, no. of live births, no. of abortion, no. of NVD and no. of CD and lower abdominal operations), working history (housewife, day laborer, official and student) and main posture during work (sitting, standing, bending and lifting).

The 2nd part of the questionnaire consisted of LBP related questions: location, intensity, radiating to the leg, duration, past H/O LBP and frequency, aggravating factors, relieving factors, and H/O stop working during episodes of LBP. A total 750 patients were found to have low back pain during this period, and 415 patients were included in the study.

The inclusion criteria were as follows: i) female, ii) within the reproductive period and iii) aged 18 to 55 years.

The exclusion criteria were as follows: i) pregnant and ii) malignant.

The data were analyzed with SPSS 25.0 statistical software, MS Word and Excel version 2010. Descriptive statistics were analyzed, i.e. - frequency, central tendency (mean, median and mode) and dispersion (range, standard deviation and variance). Tests of "proportions" and "significance" were performed via sample t-tests and ANOVA. Statistical data analysis was used to evaluate the correlation of LBP incidence and intensity (%) with age, BMI, disease status, marital status, obstetric history, working history and posture of reproductive age women.

Data analysis

In the northeastern region of Bangladesh, at the Sylhet Division in the last three (03) years (2020-22), we included 415 reproductive-aged women with low back pain (LBP) without pregnancy. The age limit of the patients was 20 to 55 years. The mean age (±SD) was 36.12 (±9.578) years (n=415). The height ranged from 138-162 cm and their weight ranged from 42-79 kg. The mean height (±SD) was 154.10 (±4.100) cm and the weight (±SD) was 59.07 (±6.646) kg. The minimum BMI was -20.0 kg/m², the maximum was -34.7 kg/m² and the mean (±SD) BMI was 24.879 (±2.832)kg/m². According to their BMI, the patients (n-415) were classified as follows: normal wt. -81.9%; overweight -5.3%; and obese -12.8%. More than 7.3% of the individuals in the 20-30 age groups were obese.

The marital status of the patients was as follows: married -75.2%; > one marriage -5.1%; widowed -4.1%; and unmarried -15.7%. The marriage age of the patients from 18-26 years, mean (\pm SD) was 21.67

(± 2.107) years; Marriage duration was 1-36 years, mean ($\pm SD$) was 16.77 ($\pm 9,372$) years; No. of pregnancy was from 0-6, mean ($\pm SD$) was 2.54 (± 1.252); No. of live birth was from 0-3, mean ($\pm SD$) was 2.33 (± 2.388); No. of abortion was 0-3, mean ($\pm SD$) was 0.33 (± 0.575) and No. of NVD was from 0-5, mean ($\pm SD$) was 2.13 (± 0.986). RAD due to CD and lower abdominal operations was -8% (minimum -1 and maximum 4) (n=415); CD, -2.9%; >1, -1.4%; LA operations, -2.9%; and both CD and LA operations -0.7%.

The medical history of the patients (n=415) was as follows: HTN -10.4%; DM -12.5%; UTI -39.8%; PID -14%; RAD -7.7%; Arthritis -8%; PLID -1.7%; Renal stones -0.7% and psychological disorders -5.3%. The working history (n=415) included the following: housewife, -42.2%; day laborer, -28.2%; official, -16.6% and student, -13%. The main working postures included standing, -26.5%; sitting, -54.5%; bending, -10.6%; and lifting, -8.4%. The prevalence of disease was -6.5% for HTN and -10.5% for DM, in the 41-50 years age group; 28% for UTI, in the 20-30 years age group; 8.5% for PID, in the 31-40 years age group; 3.5% for RAD, in both 31-40 and 41-50 years age group; 4.5% for arthritis, in the 41-50 years age group; 1% for PLID, in the 41-50 years age group; and 3.2% for psychological disorders, in the 20-30 years age group.

We estimated the incidence of LBP with a 95% confidence interval (CI) and set p<0.05 for all statistically significant relationships. [P<0.05 is significant, which indicates that the parameters have no effect on LBP in every patient; however, for some patients, have the effect (H_0), p>0.05 is not significant, which indicates that the parameters have an effect on LBP in every patient (H_0)]

One sample t-test: revealed the following: patient age, age at marriage, duration of marriage, no. of pregnancy, no. of live births, no. of abortions, no. of vaginal deliveries, working history, posture while working, patient BMI and medical history; all p-values (supplemental 2-tailed) were 0.000. The p-value was <0.05. Therefore, the parameters had *no effect on LBP* incidence in any of the patients, but had effect for *some times* of *some patients*, with the 95% confidence interval (Table 1).

Table I One-sample t-test of the parameters on LBP

	Test Value = 0								
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference				
					Lower	Upper			
Patient`s age	76.823	414	.000	.000	35.2	37.04			
Age of marriage	192.479	349	.000	.000	21.45	21.9			
Duration of marriage	33.467	349	.000	.000	15.78	17.75			
No. of pregnancy	37.959	349	.000	.000	2.41	2.67			
No. of live birth	42.395	349	.000	.000	2.11	2.31			
No. of abortion	10.776	349	.000	.000	0.27	0.39			
No. of vaginal delivery	40.392	349	.000	.000	2.02	2.23			
Working history	38.746	414	.000	.000	1.9	2.11			
Main working posture	48.584	414	.000	.000	1.93	2.09			
Patient's BMI	178.923	414	.000	.000	24.606	25.153			
Medical history	38.434	414	.000	.000	3.44	3.81			

Paired sample t-tests: were used to analyze patient age and medical history. The t-value was 66.996 and the p-value (supplemented 2-tailed) was 0.000. The p-value was <0.05. Therefore, patient *age and diseases* (HTN, DM, UTI, PID, RAD, arthritis, PLID, renal stone, and psychological disorders) *had no effect on LBP*, but *some patients had effect on LBP with age and diseases* with the 95% confidence interval.

One way ANOVA: revealed that for the patients (HTN, DM, UTI, PID, RAD, arthritis, PLID, renal stone, and psychological disorders), the mean disease incidence was 32.499 (SD=9.882), the F-value was 2.056, and the p-value (Sig.) was 0.001. The p-value was <0.05. Therefore, above mentioned diseases had no effect on LBP in all of the patients, but in some patients had an effect with the 95% confidence interval (Table 2).

Table 2 One way ANOVA between patient's Age and Diseases effect on LBP

ANOVA							
Medical history	Sum of Squares	df	Mean Square	F	Sig.		
Between Groups	237.085	34	6.973	2.056	0.001		
Within Groups	1288.52	380	3.391				
Total	1525.605	414					

Two way ANOVA (Tests of Between-Subjects Effects): Medical history (diseases), age groups, BMI groups and Age -BMI groups; the F-values are 0.862, 0.781 and 3.260, and the p-values (Sig.) are 0.461, 0.459, and 0.012. The p-value was >0.05 for age groups, BMI groups for Medical history (Diseases) but there was <0.05 between age groups and BMI groups for diseases. Therefore, diseases had relation to patient age and BMI, but there was no relation found between the age groups and BMI groups of the diseases with the 95% confidence

intervals (CIs). In the study, we found the prevalence of LBP with different age groups, BMI groups and diseases but not for all patients (Table 3).

Paired sample t-tests: were used to analyze patient working history and main Posture during work; the "t" value was -0.077, and the p-value (supplemented 2-tailed) was 0.938. The p-value was >0.05. So, working history and posture affect low back pain of all patients with 95% confidence interval (Table 4).

Table 3 Two way ANOVA (Test of Between-Subject effect on LBP)

Tests of between-subjects effects Dependent variable: Medical history							
Corrected Model	132.894 ^a	9	14.766	4.294	.000		
Intercept	972.864	1	972.864	282.909	.000		
Age Group	8.897	3	2.966	0.862	0.461		
BMI Groups	5.373	2	2.686	0.781	0.459		
Age Group * BMI Groups	44.841	4	11.21	3.26	0.012		
Error	1392.711	405	3.439				
Total	6969	415					
Corrected Total	1525.605	414					

a. R Squared = .087 (Adjusted R Squared = .067)

Table 4 Paired Samples Test between working history and working posture

	Paired differences								
	Mana	Std.	Std. Error	95% Confidence Interval				Sig.	
	Mean	Deviation Mean		Lower	Upper	- τ	df	(2-tailed)	
Pair I Working history- Main posture during work	-0.005	1.268	0.062	-0.127	0.118	-0.077	414	0.938	

Pathophysiology of LBP

LBP arises from many potential anatomical structures, i.e., nerve roots, muscles, fascial structures, bones, joints, intervertebral discs (IVDs), abdominal and pelvic viscera. The complex anatomy of lumbar spine is made up of a strong vertebral body. IVDs are linked by joint capsules, ligaments, tendons and muscles; all of these structures are potential sources of LBP. Palan The lumbar spine carries most of the body wt. which triggers symptoms of both movement and inactivity. Pain may worsen after standing or sitting for prolonged periods of time.

Structural damage, **degenerative changes**: (due to pressure load, diminished blood supply by vessel atherosclerosis) and the accumulation of pain stimuli (i.e.- nitric oxide release from granulation tissue and inflammatory cell infiltration) in lumber region tissues are the causes of LBP. The dorsal root ganglia are thought to be the main modulators of LBP. ¹⁹ Body load (wt.) transmission through the vertebral column is another precipitating cause of LBP. The weights of the upper limbs and thoracic cases were transmitted through the ribs to the posterior column of the cervical vertebra via the costotransverse joints and ligaments. The weight is transmitted through 3 columns

(one anterior and two posterior) in the cervical region whereas the weight in the thoracolumbar region passes through 2 columns (one anterior and one posterior, and both columns are run parallel to each other following the thoracolumbar curvature). In the thoracic region, wt. passed from the posterior to the anterior column due to anterior concavity of the spine through inclined pedicles, and in the lumber region, for the posterior concavity, the compressive weight dispatches from the anterior to posterior column. Therefore, the compressive force in the curvilinear thoracolumbar column tends to deviate toward the gravitational line, which is related to pathological disorders of the spine and LBP. 21 The neural arch at the $\rm L_4$ and $\rm L_5$ levels is involved in the transmission of a considerable load. Therefore, the joints between the articular facets of $\rm L_4$ and $\rm L_5$ are sites of LBP.

Prevalence of LBP (Global & Local)

Low back pain (LBP) is one of the most common physical problems and has a high socioeconomic impact, leading to working disability and poor quality of life. 10,22 The prevalence of LBP is approximately 23% in adults and the annual incidence is approximately 15%. 2.19 LBP is influenced by psychological factors, such as stress, depression and/or anxiety. 19

According to a global review in 2000, the prevalence of LBP ranged from 12-33%. 29.4% for males and 35.3% for females.^{4,23} The average incidence of LBP is 61.5% among women in Finland, Poland, Spain and India.²⁴ The incidence of back pain in one (1)-month period was reported to be 29%. Of these 20% were considered chronic and 40% was disable.²⁵ In Bangladesh, the weight related incidence of LBP is 18.5%, and that of individuals aged 18-34 years incidence are 10.5%; aged >55 years incidence are 27.8%, and average 19.2%, which is greater in women (27.2%) than in men.²

Trauma is the major cause of acute LBP, but chronic and persistent LBP are more prevalent with systemic diseases and psychological factors, such as – stress and limited health care education. ^{2,26} LBP in women can be divided into 2 main categories: i) Musculoskeletal and Nervous system causes, such as trauma, poor mobility, posture, sciatica and arthritis; and ii) other organ system based conditions, such as reproductive, kidney, infection and inflammation. ²⁷

Discussion

Low back pain can be caused by invasion of many local and systemic diseases affect the back musculoskeletal structures. The etiology of LBP is multifactorial.^{3,9} Pain is likely a dull, constant to sudden, sharp pain that may radiate to the lower limb. The pain attack may be sudden, acute, gradually aggravated or recurrent. Twenty-one percent of women develop long term LBP due to a lack of healthy lifestyles (HLSs).²⁸ Lifestyle factors, i.e. nonsmoking, physical activity, diet and moderate alcohol consumption, influence the risk of several diseases, e.g. - cancer, DM and CVD. HLS has a positive influence on the development and prognosis of LBP in women, but there is no clear association in men.²⁸

LBP is more common in women, probably due to household activities; a greater frequency of visceral pain during menstruation, pregnancy and labor, and a lower pain threshold than in men because the gonadal steroid hormones estradiol and testosterone are moderately sensitive to pain and analgesia.²⁹ Low back pain in women is linked to hormonal and reproductive factors e.g. menstruation, use of contraceptives (hormones and intrauterine devices), hysterectomy, pregnancy, obstetric history and systemic diseases.

Approximately 69% of women experienced menarche at 12-14 years of age. Menarche at the age ≤11 years and an irregular or prolonged menstrual cycle were associated with chronic LBP.30 Premenstrual syndrome (PMS) starts before menstruation and ends after the cycle. Many women develop LBP during PMS; Nikhil Jain, neurosurgeon, University of Louisville in Kentucky, said the correlation is not fully understood but is linked to hormonal changes during menstruation and mental stress.¹⁵ Premenstrual dysmorphic disorder (PMDD) is the same as PMS, but the conditions are more severe. There is a family H/O depression, and the brain reacts abnormally to hormonal changes during the menstrual periods. 15,16 Dysmenorrhea is painful menstruation. The patient experienced pain in the lower abdomen, lower back, hips and legs. When endometrial tissue grows outside the uterus in other pelvic organs, this disease is called endometriosis, and can cause pain in the pelvis and lower back, the pain is experienced in menstrual cycle, during and after sex, even during urination.

Low back pain is common during pregnancy due to a shift in the center of gravity. Rahul Shah, MD, spine surgeon, New Jersey, 15 reported weight gain; hormonal and mechanical changes during pregnancy and labor cause muscle and ligament relaxation and lead to, sacroiliac joint dysfunction. Huang noted that this pain is the main

cause of LBP.¹⁵ Additionally, sleep disturbance and mood changes during pregnancy are the result of LBP.¹ A study in the Netherlands showed that 10% of women suffer chronic LBP at the onset of pregnancy.³⁰

Back pain is common in patients with premenstrual syndrome. During menopause, a dramatic decrease in estrogen causes osteoporosis and mood changes, leading to LBP. Muscle spasm in the back causes LBP due to strain resulting from exercise, dehydration, heavy lifting or sudden absurd twists and turning of the body, as explained by Jake Magel, physiotherapist, University of Utah. Salt Lake City.

LBP indicates that pain occurs in the back between the lower costal margin and above the inferior gluteal folds.^{2,10} Pain can be specific or nonspecific. Specific LBP can be caused by disease, structural problems in the spine or pain radiating from another part of the body. There was nonspecific LBP due to unidentified causes, which was approximately 90%.¹⁰

Note for Table 5: The P-value of patient Age is <0.05 (P=0.000), so age is no factor for LBP, it can be affect at any age; LBP in the different Age Groups was (20-30 yrs. 34.2%, 31-40 yrs. 27.2%, 41-50 yrs. 34.7% & >50 yrs. 3.9%), the p-value is >0.05 (P=0.461), so different age groups has effect to LBP in reproductive women. LBP are more common in 20-30 yrs. and 41-50 yrs. age groups. Height and weight has impact on BMI, which affect LBP. Specific height and weight has no effect on LBP. The mean BMI is 24.879 (±2.833) of the patients and P-value < 0.05 (P=0.000), So BMI is not co-morbid factor for LBP in all patients but BMI subgroups P-value is >0.05 (P=0.459), so it has an effect on LBP. In our study LBP more in normal wt. patients (81.9%) but in several study found LBP are more in over wt. & obese peoples, which also increase pain intensity.^{24,25,31} We found various systemic diseases as a cause of LBP in our patients. The P-value of Disease Sub Group (HTN, DM, UTI, PID, RAD, arthritis, PLID, renal stone, and psychological disorders) is <0.05 (P=0.001), so the diseases has no impact on LBP in all patients but is the cause in some patients. Marriage history (marital status, marital age and marriage duration), Obstetric history (no. of pregnancies, no. of live births, no. of abortion and no. of NVD) and Lower abdominal operations (LAOs) of reproductive women (no. of CD and LA operations) always are not the cause of every LBP women but in the study we found those parameters affect LBP of some patients. The P-value of those parameters are <0.05 (P=0.000). LBP is more common in single married women (75.2%) but age at marriage and duration had no direct effects. Parameters of obstetric history and LAOs are not the causes of LBP in every women but some literatures mention those parameters are the cause of LBP and we also observed the same causes in some patients.3,4,17,30,32-36 Working history has no direct effect on LBP, P-value is <0.05 (P=0.000) but it is directly related to *Posture*, which has strong association with LBP, the P-value is >0.05 (P=0.938). In the study, housewives (42.2%) are more affected and those are working in sitting posture for long times (54.5%)^{2,3,7,36–38}

The risk and incidence of LBP increase with age. Individuals aged 40-49 years are more vulnerable to LBP globally.^{2,24} Among women aged 20-59 years, the prevalence of chronic LBP was 8.9% and among women aged 50-59 years, the prevalence of LBP was 42% on average in China, Russia, S. Africa and India.^{30,24} In our study, the prevalence of LBP was 34.7% in the 41-50 years age group and 34.2% in the 20-30 years age group. The mean age (±SD) was 36.12 (±9.578) years (n=415). A Brazilian study reported that the incidence of LBP in individuals aged 20-35 years was 26.4% and that in individuals aged 36-59 years was 32.7% in 2019.³⁶

Table 5 Parameter statistics for women of reproductive age (without pregnancy) with LBP

Causes of LBP (parameters)	Percentage (%) with range (N)	Mean (±SD) with 95% CI	P-value
Age	20-54 yrs. N = 415	36.12 (±9.578)	(Sig. 2-tailed) P = 0.000
Age groups			
20-30 yrs.	34.20%	2.08 (±0.916)	P = 0.461
31-40 yrs.	27.20%		
41-50 yrs.	34.70%		
>50 yrs.	3.90%		
Height	138-162 cm, N = 415	154.10 (±4.100)	-
Weight	42-79 kg, N = 415	59.07 (±6.646)	-
BMI	20-34.7 kg/m2, N = 415	24.879 (±2.833)	(Sig. 2-tailed) P = 0.000
BMI groups	•		,
Normal wt.	81.90%	N = 415	
Over Wt.	5.30%	2.31 (±0.685)	P= 0.459
Obesity	12.80%	(,	
Diseases			
HTN	10.40%	N = 415	P = 0.001
DM	12.50%	3.62 (±1.920)	. 0.001
UTI	39.80%	2.02 (21.720)	
PID	14%		
RAD	7.70%		
Arthritis	8%		
PLID	1.70%		
Renal stone	0.70%		
Psychological	5.30%		
Marital status	15 700/	N. 415	(C: 2 : 1 I)
Unmarried	15.70%	N = 415	(Sig. 2-tailed)
Married	75.20%	1.3 (±0.764)	P = 0.000
>1 married	5.10%		
Widow	4.10%		
Age of marriage	18-26 yrs. (N = 350)	21.67 (±2.107)	(Sig. 2-tailed)
Duration of marriage	1-36 yrs. (N = 350)	16.77 (±9.372)	P = 0.000
Obstetric history			
No. of pregnancy	0-6 (N = 350)	2.54 (±1.252)	(Sig. 2-tailed)
No. of live birth	0-3 (N = 350)	2.33 (±2.388)	P = 0.000
No. of abortion	0-3 (N = 350)	0.33 (±0.575)	
No. of NVD	0-5 (N = 350)	2.13 (±0.986)	
Lower abdominal operation			
CD	2.90%	N = 33	(Sig. 2-tailed)
>I CD	1.40%	2.18 (±1.044)	P = 0.000
LA operation	2.90%		
Both CD & LA operation	0.70%		
Working history	42.200/	N. 415	(C) 2
Housewife	42.20%	N = 415	(Sig. 2-tailed)
Day laborer	28.20%	2.00 (±1.054)	P = 0.000
Official Student	16.60%		
Student	13%		
Working posture	27.509/	NI = 415	(C:= 2 +=: -)
Standing	26.50%	N = 415	(Sig. 2-tailed)
Sitting	54.50%	2.01 (±0.843)	P = 0.938
Bending	10.60%		
Lifting	8.40%		

Several studies have shown that overweight and obesity increase LBP development, severity and disability. A BMI ≥25 kg/m² is a risk factor for LBP, and a BMI ≥30 kg/m² is 1.22 times greater in women.^{24,25,31} The incidence of LBP was significantly greater in women with a BMI \geq 30 kg/m² than in those with a BMI \geq 20-29 kg/m^{2,3} Globally, approximately 20-25% of adults are obese.³⁹ We calculated BMI using the BMI calculator in accordance with the International System of Units (SI). BMI was calculated as body weight in kg divided by height in cm; the unit is kg/m² and BMI varies according to age. BMI: 18.5-25, normal; 25-30, overweight and above 30, obese. 40 Obesity (OB) results from a poor lifestyle and can lead to LBP. Loss of body trunk and lower limb muscle mass and central OB are risk factors for LBP.41 Our study revealed that 5.3% of overweight and 12.8% individuals aged 20-30 years with LBP were obese (Figure 1). Body wt. increases direct vertebral compressive load and anterior acting loads. These loads act through muscles of the back that produce joint reaction forces, which lead to back pain. A body weight of 65±10 kg was significantly associated with increased LBP.3 OWs and OBs increase the risk of LBP. 42,43

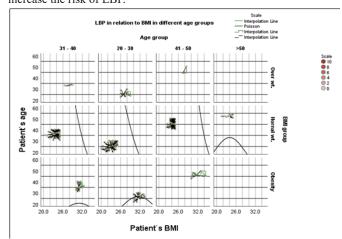


Figure I LBP in relation to BMI in different age groups.

LBP was more common among married women (78%) and unmarried women (22%).³² Patients who are married at a late age (30-34), have ≥2 children or have ≥2 abortions are at risk of LBP.³ A Brazilian study reported, LBP in married women was 43.6%%, unmarried 23.6% and widow women 32.7%.³⁶ Patients marital status was: married-75.2%, unmarried-15.7%, married more than once-5.1% and widowed-4.1%. The prevalence of stress urinary incontinence (SUI) was 60% in the LBP group. Overall 78% of the adult women reported urinary incontinence (UI) due to LBP.³⁵ The incidence of SUI is greater in married women with LBP, and there are associations between SUI and both core muscle endurance (CME) and LBP in married women.³⁵

The incidence of LBP was greater among the late marriage age group, which was observed between 32-34 years of age; this was because the obstetric risk was greater.³ In this study 17.8% of the patients were married at the age of 23 years, 13.3% were married at the age of 20 years. The mean (\pm SD) was 21.67 (\pm 2.107) years. In our study, for patients with a marriage duration ranging from 1-36 years, the mean (\pm SD) was 16.77 (\pm 9,372) years. Use of contraceptives: Many health care professionals believe there is an association between oral contraceptive use and LBP, but there is no scientific evidence supporting this association. The use of oral contraceptives are increase relaxin levels, causing laxity of ligaments and joints, and leading to LBP.³⁰ The use of intrauterine contraceptive devices may lead to LBP. LBP was more common among women who were married at a later age (30-34), had \geq 2 children or had \geq 2 abortions.³

No. of pregnancy: Relaxin is a hormone produced during pregnancy. Increased relaxin levels during pregnancy can cause laxity of ligaments and joints, leading to LBP. ³⁰ Ligaments and joint laxity due to hormonal changes, weight (wt.) gain and a shift in the center of gravity cause lumbar spine hyperlordosis with anterior tilting of the pelvis. Vascular changes may lead to compromised metabolic demand in back tissues, all of which occur during pregnancy and lead to LBP.³³ In this study, the women with LBP had 0-6 pregnancies per H/o and the mean (±SD) was 2.54 (±1.252) times.

There was an association between a greater number of live births and LBP. The Approximately 74% of women take their 1st baby between 20-30 years of age. A first birth at a young age (fibromyalgia), especially at younger than 20 years of age, Late maternal age; ≥ 2 children (pelvic joint syndrome) and a long length of time between childbirths were associated with LBP in middle aged women. The number of live births in our study ranged from 0-3 and the mean (±SD) was 2.33 (±2.388). There were 2 live births (35.9%) and 3 live births (24.8%) in the LBP group. A study revealed a linear association between the number of live births and chronic LBP. 17,30

The number of abortions ranged from 0-3, and the mean (\pm SD) was 0.33 (\pm 0.575). A total of 19.5% of women who suffered from LBP after one abortion, were included in this study. The incidence of LBP observed in \geq 2 abortions was 80%, with one occurring in 51.3% of women and 26.3% occurring in women without abortion in an Indian study.³

The prevalence of LBP was 60% in women who underwent ≥2 vaginal deliveries, 46.15% in women who underwent one delivery and 12.5% in women who did not delivery.³ In our study, two (36.6%) and three (24.6%) patients in the NVD cohort had LBP. Numbers of NVDs 0-5, and the mean number of NVDs was 2.13 (±0.986).

Rectus abdominis diastasis (RAD) is a condition; in which rectus abdominis muscles are separated by more than 2 cm. The prevalence of RAD is 30-46.5% in pregnant and postpartum women. Pregnancy, abdominal surgery and heavy lifting status are potential factors for developing RAD. In women, RAD development is 1.9 times greater than that in men, and one set occurs earlier. Women who underwent cesarean delivery (CD) or a lower abdominal operation had a 4.5 times greater risk of RAD than did those, who did not. The prevalence of LBP in women with RAD is 24-69%.34 Adhesions of abdominal and pelvic viscera were noted in CD patients and abdominal surgery patients. RAD onset occurred more often in patients aged 30-40 years. In our study, LBP developed in 2.9% of CD patients, 2.9% of LA operation patients and 7.7% of RAD patients. RAD development in the 31-40 year age group was 3.5%, and that in the 41-50 year age group was 3.7%. A total of 24.6% of the RAD patients were diagnosed with LBP in 2021 in a study by Harvard Medical School, Boston.^{4,34}

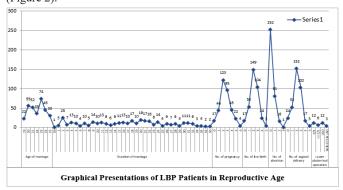
A Brazilian study was published in 2019; LBP was associated with HTN -(42.8%), DM -(19.1%), depression -(11.1%) and renal disease -(8.2%). 36

LBP and comorbid conditions such as hypertension, diabetes etc. is vice versa. LBP causes inactivity and a lack of exercise, resulting in weight gain and the subsequent development and enhancement of HTN and DM. In contrast, HTN exacerbates disc degeneration. A study at Hong Kong University revealed that 35.5% of HTN patients had moderate to severe disc degeneration. Action (cholesterol, triglyceride) are associated with LBP. HTN and DM cause atherosclerosis of the lumber vessels. Both of these conditions are highly causes of LBP. In our study, the prevalence of LBP due to HTN was -10.4%; among those aged 41-50 years, -6.5% had LBP due to HTN (Figure 3).

LBP in diabetes patients is multifactorial. Diabetes causes peripheral vascular diseases and neuropathy, and leads to chronic LBP. Diabetes causes obesity due to metabolic disturbance. OB exacerbates persistent inflammatory conditions. Moreover OA cartilage is more reactive to pro-inflammatory stress. DM causes multifactorial effects and disc degeneration; and leads to LBP.⁴⁶ LBP with DM occurs in 12.5% of women during the reproductive period. The prevalence of LBP in patients aged 41-50 years was greater (10.5%) in this study.

Urinary tract infection (UTI) causes LBP.^{47,48} UTI causes LBP and groin pain in women.²⁷ In our study, the prevalence of LBP in women with UTIs was -39.8%, and the prevalence in women aged 20-30 years was -28%. UTIs are more common in nulliparous women.⁴⁹ UTI is the leading cause of acute pelvic pain and occurs in approximately 20% of women each year. Gram-negative bacteria, especially -*E. coli*, are 80% of all UTIs.⁴⁹⁻⁵¹ The major mediator of urinary bladder inflammation is lipopolysaccharide (LPS)/ endotoxin in the outer membrane of gram-negative bacteria. Post-UTI pain can be caused by the "O"-antigen.⁵⁰

LBP is the primary symptom reported by patients with confirmed UTIs; the prevalence of UTIs during gestation was 37.5%, and the prevalence of LBP in patients aged 20-29 years was 67%.51 Approximately 48% of women have at least one episode of UTIs; women are more susceptible to UTs because they have a shorter urethra and urethral meatus close to vagina and anus. The UTI prevalence in patients with previous NVD was 72%, whereas that in patients with CD was 28%. Approximately 80% of women had UTIs with no experience of abortion, 8% had one abortion, and 12% had ≥2 abortions. The prevalence of LBP in women diagnosed with UTIs was -84.8%.⁵¹ Approximately 60% of women suffer at least one tine UTI during their life, 20-30% have repeated infections, and the UTI incidence is 16.8% among adults in Bangladesh. UTI is a risk factor for urinary incontinence (UI).52 There are associations between LBP and SUI, core muscle endurance (CME) and LBP in married women (Figure 2).35



 $\textbf{Figure 2} \ \text{Graphical presentations of LBP patients in reproductive age}.$

Pelvic inflammatory disease (PID) is inflammation of the upper genital tract in women due to infection and 85% of infections caused by STD.^{27,53} PID is more common in women aged 15-25 years. It causes LA pain and pelvic discomfort. Eighteen percent of patients develop chronic pain due to inflammation, scarring and adhesion from the infection process.²⁷ Inflammation is a sequela of infection and causes acute LBP.⁴⁷ PID causes chronic pelvic pain, scarring and adhesion, which leads to the development of LBP. The present study showed that 14% of women had LBP due to PID; the age range from 31-40 years was more prevalent at -8.5%.

LBP without medical or psychological problems, with clinical findings of i) mobility impairment in the lumbar region, ii) radiating

pain to the lower limb and iii) a positive straight leg raising (SLR) test is a clear indication of LBP due to PLID.⁹ The prevalence of PLID is 60% for males and 40% for females. The incidence was greater in the 36-45 years age group (49.42%). The lumbar spine carries most of the body weight. PLID most commonly occurs at L3/4 is 39% and at L4/5 is 18%.⁵⁴ A study in Bangladesh showed that the prevalence of LBP due to PLID is 1.9% in men and 7.6% in women. MRI revealed that posterior bulging of the intervertebral disc at the L4/5 level was due to facet-flaval hypertrophy.⁵⁵ In our study, the incidence of PLID was -1.7%, and that of more common diseases in the 41 to 50 years age group was -1%.

Arthritis causes LBP; age, overweight status and pressure on joints can lead to arthritis. Overall, 26.2% of osteoarthritis patients have a lifetime incidence of LBP.⁴⁵ Degenerative spondylolisthesis typically occurs at L4-L5 and is more common in women.³³ In OA, degenerative changes cause LBP. According to the Arthritis Foundation, approximately 20% of people have LBP. Lumber OA is very common, affecting approximately 30% of males and 28% of females; aged 55-64 years in the USA.¹² In this study, the prevalence of arthritis was 8% and patients aged 41-50 years were mostly affected (approximately 4.7%).

Renal stones (both kidney and ureteric stones) cause severe acute LBP.⁴⁸ When kidney stones move to the bladder, they are typically painful to the back and side and can radiate to the groin.²⁷ The incidence of LBP was -0.7% due to renal stones and the prevalence in the 41-50 years age group was 0.5% in this study.

There is an association between LBP and depression.24 Psychological factors, i.e. job satisfaction, social relations and mental overstrain have been associated with LBP.56 Sleep problems, low mood and increased mental distress are effects of LBP and vice versa.¹⁰ There were significant associations between disability and depression, anxiety, insomnia and sleep quality. Fifty four percent of patients reported poor sleep quality with LBP, and 30% had insomnia.³² Psychological factors, i.e. fear, low mood, expectation of passive treatment and negative pain beliefs, are risk factors for LBP. It is proposed that physiological pain resulting from organic insult; may have negative effects on emotions and cognitive function; conversely, a negative emotional state can lead to increased pain through the central pain pathway.⁵⁷ Chronic LBP has both organic and psychological factors. In our study, the incidence of LBP in women of reproductive age other than pregnancy was -5.3% and the incidence was greater in the 20-30 years age group (by -3.2%) (Figure 3).

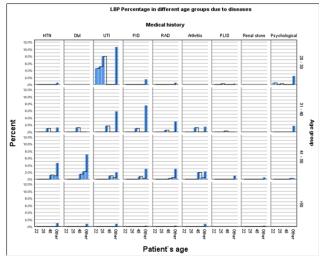


Figure 3 LBP percentages in different age groups due to underline diseases.

Working posture has a strong association with LBP incidence. Back pain in certain postures is due to the creation of high stress on spine structures.⁷ Patients who work in a standing position for long periods of time are more susceptible to LBP.3 Patients with tissue trauma and muscle spasm are more likely to be in the standing position after long term work. Approximately 83% of gynecologists suffer from back pain while performing surgery in a sitting position,, and 78% experience back pain while performing surgery in standing position.³⁷ In our study, 42.2% of the women housewives, 28.2%, 16.6% and 13% were day laborers, officials and students, respectively. The main working postures were standing -26.5%; sitting -54.5%; bending -10.6% and lifting -8.4%. LBP prevalence during work at sitting posture was 67.3%, standing 74.5% reported in Brazilian study in 2019.36 In Bangladesh, there is a positive incidence of LBP in housewives.² In the USA, LBP was significantly related to occupation in a study of people involved in lifting, carrying, pulling, pushing and twisting. In EU countries, the effect of LBP involves heavy weightlifting (≥25 kg).^{2,3,38} We found that the incidence of LBP is greater among housewives and individuals who are working in a sitting position (Figure 4 & Table 6).

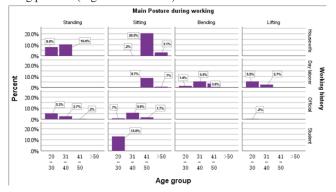


Figure 4 Main postures during work.

Table 6 Working history & posture

Working history & Posture								
Housewife		Day laborer			Official			Student
175		117		69		54		
Standing	Sitting	Sitting	Bending	Lifting	Standing	Sitting	Lifting	Sitting
76	99	39	44	34	34	34	1	54

The Roland Morris Disability Questionnaire provides a tool for measuring the level of disability experienced by a person suffering from LBP; it is widely used to measure the outcome of LBP. The questionnaire consists of 24 statements, i) physical ability/activity -15, ii) sleep/rest -3, iii) psychological -2, iv) household management -2, v) eating -1 and vi) pain frequency -1.58 The Roland-Morris Disability Questionnaire score has a moderate to strong correlation with pain intensity. The Oswestry Disability Index (ODI) is the gold standard for measuring disability and quality of life (QoL) impairment in adults with LBP. The ODI criteria for assessing functional impairment were pain intensity; ease of personal care; lifting, working, sitting, standing and sleeping; sexual life; social life and traveling. The index consists of 10 questions, which are scored from 0 to 5, and the total score is multiplied by 2; to convert the total score into a percentage. Scores are as follows: 0-20, minimal disability; 21-40, moderate disability; 41-60, severe disability; 61-80, crippling back pain; and 81-100, bedbound or exaggeration of symptoms.⁵⁹ The Bangla Health Assessment Questionnaire-Disability Index (HAQ-DI), was used to determine disability scores in Bangladesh.2 All of the above indices are used to survey for LBP in generalized or specific populations. However, all the data in this study were obtained from patients treated by us. Therefore, we measured pain intensity and disability by the Numeric and Categorical Pain Scale and clinical examination. The number 0-10 is the NRS score. 0=none, mild=1-3, moderate=4-6, severe=7-10. On the categorical scale, no pain, hurts a little, hurts slightly more, hurts even more, hurts a whole lot and hurts worst according to facial expression.

The diagnosis was made according to detailed medical and working history, careful physical examination; and proper investigations, i.e. routine blood and urine tests, X-ray, USG, CT, MRI etc. LBP was classified, and the underlying cause/causes were determined. Proper evaluations are obligatory to identify the causes of the underlying pathology of pain generators before starting treatment. 19,47

Approximately 80% of LBP cases persist for less than a week; if the duration is more than what is considered chronic.¹² The treatment plan was established according to the cause of LBP, and was explained and confirmed. Patient education and medications, i.e. NSAIDs and muscle relaxants, are beneficial. Bed rest should be avoided if possible.⁴⁷ Patients were referred to an opposite medical person when i) findings were suggestive of serious medical and psychological ii) activity limitations and impairments in body functions were reported and iii) symptoms were not resolved with interventions; we followed the LBP clinical practice guidelines of the American Physical Therapy Association (APTA).⁹

Summary

This retrospective, cross-sectional study was jointly conducted by Orthopedics and Gynecology Expertise in the North-East region of Bangladesh; among female patients of reproductive age for the last 3 years (2020 - 2022) at the Z&J fellows' medical institution. LBP has multiple causes. Retrospective studies are less expensive and faster. The retrospective studies in which the subjects were similar overall (LBP in women of reproductive age without pregnancy) but differed in particular in characteristics (i.e. - age, BMI, marital history, disease, obstetric history and occupation with posture) within a specific time limit (cross-sectional study) were included. In retrospective studies, there is no way to predict the prevalence of causes; rather, the prevalence of causes can be determined before patients are affected. In our study, we investigated the causes of LBP in women of reproductive age other than pregnant women: including age, BMI, local and systemic diseases, marriage history, obstetric history and working history with posture. The prevalence of LBP was greater in the 41-50 years age group (34.7%) and in the 20-30 years age group (34.2%). Moreover, overweight and obesity are associated with LBP. Overall, 5.3% and 12.8% of the patients were overweight and obese, respectively, and were aged 20-30 years with LBP. Patient age, BMI, disease status, marital status, obstetric history and working history had no effect on any of the patients, but some patients had LBP; overweight, obesity, age group and working posture had direct effects on LBP incidence (p>0.05). LBP is more common in women, possibly due to household activities; a greater frequency of visceral pain during

menstruation, pregnancy and labor and a lower pain threshold than in men because the gonadal steroid hormones estradiol and testosterone are moderately sensitive to pain and analgesia.

Conclusion

Low back pain (LBP) results from multiple physical conditions (both local and systemic) in women of reproductive age except for pregnant women. LBP disrupts the back tissues of the lumbosacral region. A diagnosis is made by a meticulous and detailed history of marriage, obstetric, medical and working care, etc. as well as by careful physical examination and proper investigations. Women are more susceptible to LBP, because of menstrual and obstetric factors. The parameters (data/causes) revealed that LBP had no effect on any of the patients, but women of reproductive age may suffer from LBP due to differences in cause.

Limitations

There are many publications on LBP, among the general population, occupations, global prevalence, different countries, and even pregnancy status. However, we found few publications on LBP in women during the reproductive period except during pregnancy. Therefore, we cannot compare our findings with those of others.

Declarations

Ethical approval: The research article was approved by local ethical committee, formed by Z and J fellows' Medical Institution. Reference no.: ZJFMI.Syl-011/2023, dated: 15.12.2023.

Consent: We obtain written permission from of Z&J fellows` medical institution for publication. All patients signed a written informed consent form for the use of their information in the publication of all media.

Data and Materials: We declare that all the collected data are original and collected by the authors from our patient computer database. All data generated and analyzed during the study, findings are included into the manuscript and also available from the corresponding author on reasonable request. No others person/institutions are not involved in the data and findings.

Conflict of interest: There are no conflicts of interest associated with this publication.

Funding: We are the authors who declare that we are free from all kinds of payments or benefits from others, even from our Z and J fellows' medical institution. All expenses were provided by the authors.

Author's contributions: 1a) Assist. Professor U. S. Bilkish; Writing, editing, data collection and review the manuscript, 1b) J. Hossain; was contribution in main writing and editing the manuscript, data collection and selection, data analysis and interpretation, literature reviews, 2) Assist. Professor Murshida Afruz; Writing and data collection, 3) C. F. Rob; was contribution in writing and editing the manuscript and data collection, 4) Assist. Professor M. G. Mustofa; data collection and review, 5) Chowdhury A. B. M. Bodrudduza; data collection.

Acknowledgments

The medical institution Z&J fellows' acknowledge us to publish this manuscript.



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