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ORIGINAL ARTICLE

Clinical, Hematological, and Histopathological Correlations in Women with Uterine Prolapse. A Multidimensional Gynecological Study

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ABSTRACT

Background: Uterine prolapse is a common gynecological condition, especially among multiparous and postmenopausal women, characterized by downward displacement of the uterus. While clinically evident, the associated systemic and tissue-level changes remain under-investigated. This study aimed to explore the clinical presentation, hematological status, and histopathological alterations in women with uterine prolapse in a multidimensional framework.

Methods: A cross-sectional study was conducted at tertiary care hospitals in Pakistan, specifically at the Burns and Plastic Surgery Centre, Hayatabad, Peshawar, and Jinnah Hospital, Lahore. A total of 100 women aged 30 to 75 years, diagnosed with varying grades of uterine prolapse classified according to the Pelvic Organ Prolapse Quantification (POP-Q) system, were enrolled. Clinical parameters such as age, parity, menopausal status, and duration of symptoms were documented. Hematological evaluations included complete blood count (CBC), focusing on hemoglobin concentration, total leukocyte count, and platelet count. Erythrocyte sedimentation rate (ESR) was assessed separately as an inflammatory marker, while C-reactive protein (CRP) was analyzed through chemical pathology. Histopathological examination of pelvic support tissues was performed in surgical cases (n=75) to evaluate fibromuscular integrity and vascular alterations.

Results: The majority of patients were between 45 and 65 years and presented with Grade III or IV prolapse. Moderate to severe anemia was found in 68% of participants. Elevated ESR and CRP were noted in 54% of patients. Histopathological analysis revealed fibromuscular atrophy in 78%, chronic inflammation in 66%, stromal edema in 64%, and vascular congestion in 59% of surgical cases. Severity of prolapse correlated with histological and laboratory findings.

Conclusion: Uterine prolapse is associated with structural degeneration, systemic inflammation, and hematological compromise. Integrated clinical, laboratory, and histological evaluation may enhance disease management.

Keywords: Uterine prolapse, histopathology, anemia, ESR, CRP, pelvic floor dysfunction, fibromuscular atrophy.

INTRODUCTION

Uterine prolapse, a form of pelvic organ prolapse (POP), remains a significant yet often under-discussed public health concern, particularly in developing countries where reproductive health services may be limited and postpartum care suboptimal. It is defined as the downward descent of the uterus from its normal anatomical position into or through the vaginal canal due to the weakening of the pelvic floor muscles, ligaments, and connective tissue support structures[1]. This condition predominantly affects multiparous and postmenopausal women, though it may occur at any reproductive age depending on risk factors such as vaginal deliveries, obesity, aging, chronic constipation, heavy lifting, and genetic predispositions that compromise connective tissue integrity[2].

Globally, the true burden of uterine prolapse is difficult to quantify due to underreporting and cultural stigma surrounding genital and reproductive health disorders. However, estimates suggest that up to 50% of parous women may experience some form of pelvic organ prolapse in their lifetime, with a substantial subset experiencing symptomatic uterine descent[3]. In low- and middle-income countries like Pakistan, delayed health-seeking behavior, limited access to gynecological services, and high fertility rates contribute to a higher prevalence of moderate to severe uterine prolapse, often presenting late with complications that affect quality of life, sexual function, urinary continence, and psychological well-being[4].

Despite being a clinically overt condition, the systemic biological responses and microscopic pathological alterations associated with uterine prolapse have not been adequately studied. The majority of clinical management strategies are based on symptom severity and anatomical grading, often overlooking the broader implications of systemic inflammation, hematological status, and underlying histopathological degeneration of pelvic support tissues[5]. Previous research has mostly focused on surgical outcomes, quality of life metrics, or anatomical staging, while very few studies have attempted to integrate laboratory-based hematological parameters or tissue-level histopathology into the clinical framework of uterine prolapse[6].

From a pathophysiological standpoint, uterine prolapse results from a failure in the normal support mechanisms of the uterus, including the uterosacral ligaments, cardinal ligaments, pubocervical fascia, and the levator ani muscle group[7]. Over time, repeated mechanical stress, estrogen deficiency during menopause, and collagen degradation contribute to fibromuscular atrophy and connective tissue laxity. These structural weaknesses may also be accompanied by chronic low-grade inflammation, impaired vascularization, and degenerative changes at the histological level. However, the extent of these alterations and their correlation with the clinical severity of prolapse have not been comprehensively examined in large-scale clinical settings[8].

Hematological parameters, such as anemia and elevated markers of inflammation like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may provide important insights into the systemic burden of disease in women with uterine prolapse[9]. Anemia, particularly iron deficiency anemia, is highly prevalent in South Asian women and may be exacerbated by poor nutritional intake, heavy menstrual bleeding, or chronic inflammatory states associated with pelvic floor disorders. Moreover, increased inflammatory markers may reflect ongoing tissue injury, immune activation, or subclinical infections, which could influence the course of prolapse and its associated morbidity[10].

Histopathological evaluation of pelvic tissues, particularly in surgically treated patients, allows direct observation of microscopic changes in muscular fibers, stromal cells, vasculature, and inflammatory infiltrates[11]. Identifying patterns such as fibromuscular atrophy, vascular congestion, edema, and chronic inflammation can help understand the degenerative trajectory of the prolapse process and guide future interventions. However, literature combining clinical symptomatology, haematological

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profiling, and histopathological evidence in a single integrated study remains scarce[12].

Given this background, the present study aims to bridge this critical knowledge gap by adopting a multidimensional approach to the evaluation of uterine prolapse. By correlating clinical presentation with haematological indices and histopathological findings, this study seeks to offer a more holistic understanding of the disease. This approach may help in identifying underlying biological markers of severity, improving diagnostic precision, and tailoring individualized management strategies for affected women. The findings are expected to contribute significantly to the current understanding of uterine prolapse in resource-constrained settings and provide a foundation for future translational and interventional research[13].

MATERIALS AND METHODS

This cross-sectional observational study was conducted from June 2022 to March 2023 across two tertiary care teaching hospitals in Pakistan: Burns and Plastic Surgery Centre, Hayatabad, Peshawar, and Jinnah Hospital, Lahore, Pakistan.These institutions were selected due to their high clinical load, availability of multidisciplinary diagnostic facilities, and established gynecological surgical services. Ethical approval for the study was obtained from the Institutional Review Boards (IRBs) of all participating centers. Written informed consent was secured from each participant after providing verbal and written explanations of the study's objectives, procedures, and data confidentiality assurance.

A total of 100 women diagnosed with uterine prolapse were enrolled through non-probability purposive sampling. Eligibility criteria included women aged 30 to 75 years, clinically confirmed to have uterine prolapse of any grade based on the Pelvic Organ Prolapse Quantification (POP-Q) system. Patients with a previous diagnosis of pelvic or gynecologic malignancy, pelvic tuberculosis, acute infections, autoimmune disease, or those undergoing immunosuppressive therapy were excluded from the study. The goal was to study uncomplicated cases of prolapse without systemic disease interference to ensure the reliability of inflammatory and histopathological assessments.

Upon recruitment, each patient underwent a comprehensive gynecological examination by senior consultants trained in pelvic floor assessment. A standardized data collection form was used to record age, parity, obstetric history, menopausal status, history of prolonged or difficult labor, and symptoms related to prolapse such as vaginal bulge, pelvic heaviness, lower abdominal discomfort, urinary frequency, urgency, or incontinence. The severity of uterine prolapse was categorized as Grade I to IV using the internationally accepted POP-Q staging system.

All patients were referred to the institutional laboratories for laboratory workup. Hematological investigations were conducted to assess systemic health and included complete blood count (CBC), which provided hemoglobin concentration, total white blood cell (WBC) count, and platelet count. The erythrocyte sedimentation rate (ESR) was measured by the Westergren method and served as an indicator of non-specific systemic inflammation. C-reactive protein (CRP), although not a hematological parameter, was measured using an immunoturbidimetric assay in the chemical pathology laboratory to provide a sensitive index of inflammation. Hemoglobin levels below 10 g/dL were considered indicative of moderate to severe anemia. An ESR of >20 mm/hr and CRP levels above 5 mg/L were interpreted as elevated based on institutional reference standards.

Histopathological evaluation was performed on pelvic tissues collected from patients undergoing vaginal hysterectomy as part of definitive surgical treatment for prolapse. Tissue samples were obtained intraoperatively from key pelvic support structures including the uterosacral ligaments, paracervical fascia, and adjacent pelvic musculature. These tissues were immediately fixed in 10% neutral-buffered formalin, processed using standard paraffin embedding techniques, and sectioned at 4-micron thickness. Hematoxylin and eosin (H&E) staining was used for light microscopic analysis. Histopathological examination was conducted independently by two qualified histopathologists who were blinded to the patients' clinical and hematological profiles to minimize observer bias. The primary histological features evaluated included fibromuscular atrophy, stromal edema, vascular congestion, neovascularization, and the presence and density of chronic inflammatory infiltrates. A semi-quantitative grading scale (mild, moderate, severe) was applied to each parameter to ensure consistent reporting.

Data were compiled and analyzed using IBM SPSS Statistics for Windows, Version 27. Continuous variables such as hemoglobin and CRP levels were expressed as mean ± standard deviation (SD), while categorical variables such as prolapse grade, anemia status, and presence of histopathological features were presented as frequencies and percentages. The distribution of continuous data was assessed using the Shapiro-Wilk test. Associations between prolapse grade and hematological or histopathological findings were analyzed using chi-square tests for categorical variables and ANOVA or independent t-tests for continuous variables. Pearson or Spearman correlation coefficients were calculated to explore relationships between inflammatory markers and prolapse severity. A p-value less than 0.05 was considered statistically significant for all tests.

RESULTS

This cross-sectional study included a total of 100 women clinically diagnosed with uterine prolapse. The participants ranged in age from 30 to 75 years, with the majority falling in the 45 to 65-year age group. The mean age of the study population was 54.8 ± 8.3 years. As shown in Table 1, the largest proportion of patients (38%) were aged between 55 and 65 years, followed by 34% in the 45-54 age group. Only 12% of patients were younger than 45 years, and 16% were older than 65. This distribution reflects the chronic and progressive nature of uterine prolapse, which tends to become more symptomatic and clinically evident in perimenopausal and postmenopausal women due to hormonal decline, pelvic tissue weakening, and obstetric trauma accumulated over the years.

Table 1: Age-Wise Distribution of Patients with Uterine Prolapse

Age Group (Years)	Frequency (n)	Percentage (%)
30-44	12	12.0
45-54	34	34.0
55-65	38	38.0
66-75	16	16.0
Total	100	100.0

Clinical grading of uterine prolapse was done using the Pelvic Organ Prolapse Quantification (POP-Q) system. As detailed in Table 2, the majority of patients presented with Grade III prolapse (42%), followed by Grade II (28%) and Grade IV (20%). Only 10% of patients had Grade I prolapse. This distribution suggests a high prevalence of moderate to severe cases in our cohort, which may reflect delayed presentation to healthcare facilities, underdiagnosis in earlier stages, sociocultural stigma, and limited access to gynecological care in many parts of Pakistan. The high frequency of advanced-grade prolapse emphasizes the chronicity and neglect associated with this condition in resource-limited settings.

Table 2: Clinical Grading of Uterine Prolapse According to POP-Q System

Prolapse Grade	Number of Patients (n)	Percentage (%)
Grade I	10	10.0
Grade II	28	28.0
Grade III	42	42.0
Grade IV	20	20.0
Total	100	100.0

Hematological analysis revealed significant systemic abnormalities. As shown in Table 3, moderate to severe anemia,

defined as hemoglobin levels below 10 g/dL, was found in 68% of the patients, indicating widespread nutritional deficiency, chronic blood loss, or both. Additionally, 54% of patients had elevated ESR (erythrocyte sedimentation rate), and 54% had raised CRP (C-reactive protein) levels. Although CRP is a chemical pathology marker, its elevation alongside ESR supports the presence of systemic inflammation, possibly due to chronic tissue strain, local ischemia, or low-grade infection in prolapsed organs. These laboratory findings were more prominent in women with Grade III and IV prolapse, suggesting that disease severity may be associated with systemic inflammatory burden.

Table 3: Hematological and Inflammatory Markers in Patients with Uterine Prolapse

Parameter	Number of Patients (n)	Percentage (%)
Moderate to Severe Anemia	68	68.0
Elevated ESR (>20 mm/hr)	54	54.0
Elevated CRP (>5 mg/L)	54	54.0

Histopathological evaluation was performed in 75 patients who underwent vaginal hysterectomy. Microscopic examination of uterosacral ligaments, pelvic fascia, and surrounding tissues revealed degenerative and inflammatory changes that correlated well with clinical severity. As shown in Table 4, fibromuscular atrophy was the most common finding (observed in 78% of cases), reflecting chronic stress and degeneration of supportive tissues due to repeated trauma and lack of estrogen support in postmenopausal women. Chronic inflammatory infiltrates were seen in 66% of specimens, suggesting ongoing local immune activation, possibly in response to mechanical irritation or ischemia. Stromal edema was noted in 64% of tissues, indicating interstitial fluid accumulation and vascular dysfunction. Vascular congestion was found in 59% of cases, supporting the hypothesis that compromised venous return and pressure buildup may contribute to histological and clinical worsening.

Table 4: Histopathological Changes in Pelvic Support Tissues (n = 75)

Histopathological Feature	Frequency (n)	Percentage (%)
Fibromuscular Atrophy	59	78.0
Chronic Inflammatory Infiltrates	50	66.0
Stromal Edema	48	64.0
Vascular Congestion	44	59.0

Collectively, these results reveal a strong correlation between prolapse severity, systemic hematological alterations, and histopathological degeneration. Women with higher-grade prolapse not only had more prominent clinical symptoms but also showed greater degrees of anemia, systemic inflammation, and irreversible pelvic tissue damage on microscopy. This reinforces the multifactorial pathogenesis of uterine prolapse, involving anatomical, systemic, and inflammatory pathways. Importantly, the study emphasizes the utility of incorporating basic hematological and histological evaluations in clinical practice to better understand disease severity, anticipate complications, and tailor surgical and rehabilitative strategies accordingly.

DISCUSSION

Uterine prolapse remains a pervasive gynecological disorder, particularly in low- and middle-income countries where women often delay seeking medical attention due to sociocultural stigma, lack of awareness, and limited access to specialized care. The findings of the current study underscore the complex interplay between clinical severity, systemic hematological changes, and underlying histopathological degeneration in women with uterine prolapse across diverse tertiary care centers in Pakistan[14].

The demographic profile of the study population aligns with previously published literature, where the majority of cases fall within the post-reproductive age group. In the present study, 72% of women were between 45 and 65 years, emphasizing the role of menopausal hormonal changes, collagen weakening, and obstetric history in the pathogenesis of prolapse[15]. The high prevalence of advanced-grade prolapse (Grade III and IV in 62% of cases) observed in our cohort highlights the chronic and progressive nature of the condition. These findings are consistent with previous studies from South Asia, which have reported delayed diagnosis and treatment due to barriers such as illiteracy, poverty, and lack of gynecological screening programs[16].

A key strength of this study is its inclusion of hematological analysis, which revealed a significant burden of anemia and systemic inflammation among women with prolapse. Moderate to severe anemia was present in 68% of cases. This is not surprising, considering that multiparity, poor nutrition, and chronic blood loss due to concurrent menorrhagia or postmenopausal bleeding are common in this population[17]. Anemia not only impairs wound healing and surgical recovery but may also reflect a systemic manifestation of chronic stress on the body due to pelvic dysfunction. Elevated inflammatory markers such as ESR and CRP were present in more than half the patients. These markers, although non-specific, may indicate underlying low-grade inflammation driven by chronic tissue ischemia, recurrent trauma, or subclinical infections within the prolapsed uterus and adjacent pelvic structures. This finding resonates with reports by Fritel et al. (2019), who suggested that systemic inflammation may accelerate tissue degradation in prolapse pathogenesis[18].

Perhaps the most significant contribution of this study lies in its histopathological findings. Among women who underwent surgical intervention, fibromuscular atrophy was the most common microscopic change (78%), followed by chronic inflammatory infiltrates (66%), stromal edema (64%), and vascular congestion (59%). These findings are in line with the results of histological evaluations reported by Zhang et al. (2017), who described similar degenerative changes in the endopelvic fascia and uterosacral ligaments[10]. Fibromuscular atrophy reflects chronic overdistension, denervation, and reduced vascular supply to the pelvic floor. Chronic inflammation, in turn, may contribute to matrix remodeling, collagen disorganization, and weakening of tissue tensile strength. Stromal edema and vascular congestion further suggest venous pooling and lymphatic obstruction, which may exacerbate local hypoxia and inflammatory cascades[19].

An important observation in this study is the apparent correlation between clinical severity and both hematological and histological parameters. Higher-grade prolapse was associated with more frequent anemia, elevated CRP and ESR, and more pronounced histopathological deterioration[20]. While this relationship does not confirm causality, it supports a model in which advancing prolapse represents a state of progressive tissue breakdown, systemic burden, and compromised pelvic perfusion. These findings argue for the importance of early detection and intervention, particularly in women with risk factors such as multiparity, postmenopausal status, and poor nutritional health[21].

From a clinical perspective, the integration of hematological screening and histopathological evaluation into routine management of uterine prolapse may offer additional value in risk stratification and surgical planning. Patients with significant anemia or inflammation may require preoperative optimization. Likewise, histological assessment post-surgery may inform recurrence risk or indicate underlying pathologies that require further follow-up[22].

Limitations of this study include the cross-sectional design, which limits causal inference, and the reliance on samples from surgical cases for histopathological analysis, potentially excluding early-stage patients who were managed conservatively. Additionally, while ESR and CRP are useful screening tools, more specific molecular markers of tissue degradation or inflammation (e.g., MMPs, IL-6) could offer deeper mechanistic insights[23].

Despite these limitations, this study is among the few in the region to holistically assess clinical, hematological, and histopathological dimensions of uterine prolapse in a single framework. The findings underscore the multifactorial nature of the disease and call for integrated strategies combining clinical

vigilance, laboratory support, and early surgical consultation to improve outcomes[24].

CONCLUSION

This multidimensional study reveals that uterine prolapse is not merely an anatomical disorder but a systemic condition with significant clinical, hematological, and histopathological implications. The findings demonstrate a clear association between the severity of prolapse and underlying fibromuscular degeneration, chronic inflammation, and systemic hematological abnormalities such as anemia and elevated inflammatory markers. Advanced stages of prolapse were found to correlate strongly with tissue-level deterioration and systemic inflammatory responses, suggesting a chronic progressive pathophysiological process. Importantly, the integration of clinical staging with laboratory and histological assessments offers a more comprehensive understanding of disease burden and progression. These results underscore the need for timely diagnosis, early intervention, and multidisciplinary management strategies especially in resource-limited settings where delayed presentation is common. Screening for anemia and inflammation, along with histopathological evaluation where surgical treatment is pursued, should be considered essential components of patient care. Future research should focus on prospective studies and molecular profiling to better understand the etiological mechanisms and identify early biomarkers for disease progression.

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