Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3004-3008 | ISSN:2251-6727

Study of Mast Cell Distributionin Uterine Smooth Muscle Tumours

Dr. Zermina Jamal, JR-3, department of pathology, Integral Institute of Medical Sciences and Research (IIMSR)

Dr. Nausheen Sanaullah Khan, Professor, Department of Pathology,IIMSR (integral institute of medical science and research),

Dr Priyanka Singh HOD , , Department of Pathology,IIMSR (integral institute of medical science and research)

Corresponding author- Dr. Zermina Jamal*

(Received: 25 October 2025 Revised: 27 November 2025 Accepted: 16 December 2025)

KEYWORDS

Distributionin
Uterine

ABSTRACT:

Uterine smooth muscle tumors (SMTs) constitute a heterogeneous group of neoplasms ranging from benign leiomyomas to malignant leiomyosarcomas, with smooth muscle tumors of uncertain malignant potential (STUMP) representing an intermediate and diagnostically challenging category. Although traditional histopathological parameters such as cytological atypia, mitotic index, and tumor cell necrosis remain central to classification, increasing evidence highlights the critical role of the tumor microenvironment in influencing tumorbehavior. Among immune components of the stromal milieu, mast cells have emerged as key modulators of inflammation, angiogenesis, extracellular matrix remodeling, and immune regulation.

This narrative review synthesizes evidence from eleven published studies between 2015 and 2025 to evaluate mast cell distribution, density, detection methods, and pathological significance across uterine leiomyoma, STUMP, and leiomyosarcoma. The reviewed literature consistently demonstrates increased mast cell infiltration in leiomyomas, often localized around blood vessels and fibrous stroma, suggesting a role in tumor growth and angiogenesis. In contrast, STUMP exhibits variable and heterogeneous mast cell distribution, reflecting its uncertain biological behavior. Leiomyosarcomas generally show reduced mast cell density compared to benign counterparts, correlating with poor differentiation and aggressive clinical course.

Collectively, these findings indicate that mast cell distribution patterns differ significantly across the spectrum of uterine smooth muscle tumors and may serve as supportive indicators of tumor differentiation and biological potential. Understanding the interaction between mast cells and neoplastic smooth muscle cells enhances insight into tumor biology and underscores the importance of the tumor microenvironment in gynecologic pathology. Further standardized, large-scale studies integrating immunohistochemistry and molecular analysis are warranted to clarify the diagnostic and prognostic relevance of mast cells in uterine smooth muscle tumors.

INTRODUCTION

Uterine smooth muscle tumors (SMTs) represent a common and clinically significant group of mesenchymal neoplasms of the female genital tract, encompassing a wide biological spectrum from benign leiomyomas to highly aggressive leiomyosarcomas, with smooth muscle tumors of uncertain malignant potential (STUMP) occupying an intermediate and diagnostically challenging category [1]. Leiomyomas are the most frequent uterine tumors in women of reproductive age and are generally associated with favorable outcomes, whereas leiomyosarcomas are rare but aggressive malignancies characterized by early metastasis, resistance to therapy, and poor prognosis [2]. STUMP poses a unique diagnostic dilemma due to overlapping histomorphological features that preclude definitive categorization as benign or malignant, thereby complicating clinical management and follow-up strategies [3].

The current classification and prognostication of uterine SMTs rely primarily on histopathological parameters, including cytological atypia, mitotic activity, and the presence or absence of tumor cell necrosis [4]. Although these criteria remain central to diagnosis, increasing evidence suggests that tumorbehavior cannot be fully explained by neoplastic cell morphology alone. The

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3004-3008 | ISSN:2251-6727

tumor microenvironment, comprising stromal cells, immune infiltrates, extracellular matrix components, and vascular elements, has emerged as a critical determinant of tumor growth, differentiation, and progression [5,6]. Understanding the interaction between tumor cells and their microenvironment is therefore essential for refining diagnostic accuracy and identifying novel prognostic indicators.

Among immune cells present within the tumor microenvironment, mast cells have gained considerable attention due to their multifunctional biological roles. Mast cells are bone marrow–derived cells traditionally associated with allergic reactions; however, they are now recognized as important regulators of chronic inflammation, angiogenesis, tissue remodeling, and immune modulation [7]. Through the release of bioactive mediators such as histamine, proteases (tryptase and chymase), cytokines, and growth factors, mast cells influence vascular permeability, extracellular matrix degradation, and cellular proliferation, processes that are fundamental to tumor biology [8].

In neoplastic conditions, mast cells have been shown to exert both tumor-promoting and tumor-inhibitory effects, depending on tumor type, stage, and local microenvironmental signals [9]. In gynecological pathology, several studies have demonstrated altered mast cell density and distribution in benign and malignant uterine lesions, suggesting a potential association between mast cell infiltration and tumor differentiation [10]. Specifically, increased mast cell density has been consistently reported in uterine leiomyomas, often with perivascular and stromallocalization, implying a role in angiogenesis and tumor growth [11]. In contrast, leiomyosarcomas generally exhibit reduced mast cell infiltration, which may reflect loss of stromal regulation and aggressive biological behavior [12]. STUMP demonstrates heterogeneous mast cell patterns, paralleling its uncertain malignant potential and variable clinical outcomes [13].

Despite growing interest in the role of mast cells in uterine smooth muscle tumors, existing studies vary considerably in methodology, sample size, mast cell detection techniques, and quantitative assessment, resulting in heterogeneous and sometimes conflicting observations. Moreover, the diagnostic and prognostic significance of mast cell distribution has not yet been standardized or integrated into routine pathological evaluation. This highlights the need for a comprehensive synthesis of available evidence to clarify the pathological relevance of mast cells within the spectrum of uterine SMTs.

The present review aims to systematically synthesize and critically analyze published literature from 2015 to 2025 focusing on mast cell distribution in uterine leiomyoma, STUMP, and leiomyosarcoma. By consolidating data on mast cell density, localization, detection methods, and biological significance, this review seeks to enhance understanding of tumor–microenvironment interactions and to explore the potential role of mast cells as supportive diagnostic and prognostic indicators in uterine smooth muscle tumors.

Methodologyof LiteratureReview

A comprehensive and systematic literature search was conducted to identify published studies evaluating mast cell distribution and its pathological significance in uterine smooth muscle tumors. The review focused on peer-reviewed articles indexed in major biomedical databases, including PubMed/MEDLINE, Scopus, and Google Scholar, to ensure broad coverage of relevant international literature. The search period was restricted to studies published between January 2015 and December 2025 in order to capture contemporary data and recent advances in tumor microenvironment research [1–3].

The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords, including “mast cells,” “uterine smooth muscle tumors,” “leiomyoma,” “leiomyosarcoma,” “smooth muscle tumor of uncertain malignant potential,” “STUMP,” “tumor microenvironment,” “angiogenesis,” and “immunohistochemistry.” Boolean operators (AND, OR) were used to refine and optimize search results for relevance and specificity [4, 5].

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

(i) original research articles, observational studies, comparative studies, or relevant review articles;

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3004-3008 | ISSN:2251-6727

(ii) studies evaluating mast cell density, distribution, localization, or functional role in uterine leiomyoma, STUMP, or leiomyosarcoma;

(iii) use of histochemical or immunohistochemical methods for mast cell identification; and

(iv) articles published in the English language with full-text availability [6–8].

Exclusion criteria comprised case reports with limited pathological data, conference abstracts, editorials, letters to the editor, non-peer-reviewed articles, animal-only studies, and studies lacking clear methodology or outcome measures related to mast cell assessment [9].

Study Selection and Data Extraction

Titles and abstracts retrieved from database searches were initially screened for relevance. Full-text articles of potentially eligible studies were subsequently reviewed in detail. From each selected study, data were extracted regarding study design, sample size, tumor subtype, mast cell detection technique (special stains or immunohistochemistry), markers used, quantitative or qualitative assessment methods, and key pathological or clinical correlations [10–12]. Comparative evaluation was performed to identify consistent patterns and variations across different tumor categories.

Data Synthesis

Given the heterogeneity in study design, mast cell quantification methods, and reporting outcomes, a qualitative narrative synthesis approach was adopted rather than meta-analysis. The findings were systematically grouped and analyzed according to tumor subtype—leiomyoma, STUMP, and leiomyosarcoma—to highlight differences in mast cell distribution and their potential diagnostic and biological significance. Research gaps and methodological limitations were also identified to guide future studies [13] .

Result

The synthesis of eleven published studies evaluating mast cell distribution in uterine smooth muscle tumors revealed distinct and reproducible patterns across the benign, intermediate, and malignant spectrum of these neoplasms. Most studies employed histochemical stains such as toluidine blue for mast cell identification and quantification.

Mast Cell Density Across Tumor Subtypes

Leiomyomas consistently demonstrated higher mast cell density compared to adjacent normal myometrium and malignant counterparts. Mast cells were predominantly localized in the perivascular regions, fibrous stroma, and intercellular spaces of leiomyomas, indicating their association with angiogenesis and stromalremodeling [14–17]. Several studies reported a statistically significant increase in mast cell counts in leiomyomas, particularly in cellular and vascular-rich variants [18,19].

In contrast, smooth muscle tumors of uncertain malignant potential (STUMP) exhibited variable and heterogeneous mast cell distribution. Some cases showed mast cell densities comparable to leiomyomas, while others demonstrated reduced counts approaching those observed in leiomyosarcomas [20]. This heterogeneity mirrored the ambiguous histopathological and clinical behavior of STUMP.

Leiomyosarcomas uniformly demonstrated lower mast cell density compared to leiomyomas. Mast cells, when present, were sparsely distributed and lacked consistent perivascular clustering [21,22]. Reduced mast cell infiltration was observed irrespective of tumor grade, suggesting a loss of stromal immune regulation in malignant transformation.

Detection Methods and Correlations

Immunohistochemical detection using tryptase and CD117 was found to be more sensitive and reproducible than histochemical staining alone. Some studies reported a positive correlation between mast cell density and microvessel density in leiomyomas, whereas such associations were weak or absent in leiomyosarcomas [23]. No uniform cutoff values for mast cell quantification were identified across studies.

Discussion

The findings of this review highlight distinct differences in mast cell distribution across uterine smooth muscle tumors, underscoring the relevance of the tumor microenvironment in influencing tumor biology. The consistently increased mast cell density observed in leiomyomas supports the hypothesis that mast cells contribute to benign tumor growth through

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3004-3008 | ISSN:2251-6727

angiogenesis, extracellular matrix remodeling, and stromal support [24].

Mast cells are known to release a wide range of bioactive mediators, including histamine, tryptase, chymase, cytokines, and angiogenic factors, which promote vascular proliferation and tissue remodeling. Their perivascular localization in leiomyomas suggests a functional role in sustaining tumor vascularity and maintaining a controlled, non-aggressive growth pattern [25]. Hormonal modulation of mast cell activity may further enhance their recruitment in leiomyomas, aligning with the estrogen- and progesterone-dependent nature of these tumors [26].

The heterogeneous mast cell distribution observed in STUMP reflects its uncertain biological behavior and supports the concept that STUMP represents a transitional category between benign and malignant smooth muscle tumors. Variable mast cell infiltration in STUMP may correspond to differing degrees of stromal interaction and immune regulation, potentially influencing clinical outcomes and recurrence risk [27]. However, the lack of standardized assessment methods limits the utility of mast cell density as an independent diagnostic marker in this category.

In leiomyosarcomas, reduced mast cell density suggests a disrupted or hostile tumor microenvironment characterized by aggressive cellular proliferation and diminished stromal regulation. Loss of mast cell–mediated angiogenic and immunomodulatory control may contribute to the aggressive behavior, invasiveness, and poor prognosis associated with leiomyosarcoma [28]. Similar patterns of reduced mast cell infiltration have been reported in other high-grade malignancies, supporting a broader role for mast cells in tumor differentiation rather than malignancy per se [29].

Despite consistent trends, interpretation of mast cell distribution is limited by methodological variability among studies, including differences in staining techniques, counting methods, and sample size. Additionally, most studies were retrospective and lacked long-term clinical correlation. Therefore, while mast cell distribution appears to be a supportive pathological feature, it cannot currently replace established histomorphological criteria.

Future research should focus on standardized mast cell quantification protocols, integration with immunohistochemical and molecular markers, and correlation with clinical outcomes. Such approaches may clarify whether mast cells can serve as adjunctive diagnostic or prognostic indicators in uterine smooth muscle tumors.

Conclusion

This review synthesizes available evidence on mast cell distribution across the spectrum of uterine smooth muscle tumors and highlights the importance of the tumor microenvironment in influencing tumor biology. Analysis of the reviewed literature demonstrates a consistent pattern of increased mast cell density in uterine leiomyomas, heterogeneous distribution in smooth muscle tumors of uncertain malignant potential, and reduced mast cell infiltration in leiomyosarcomas. These distinct patterns suggest that mast cell presence correlates with tumor differentiation and biological behavior.

The prominent perivascular and stromallocalization of mast cells in leiomyomas supports their role in angiogenesis, extracellular matrix remodeling, and maintenance of a benign tumor microenvironment. In contrast, the diminished mast cell presence observed in leiomyosarcomas may reflect loss of stromal immune regulation associated with aggressive tumorbehavior. The variable mast cell distribution in STUMP mirrors its intermediate and unpredictable clinical course, emphasizing the complexity of this diagnostic category.

Although mast cell distribution alone cannot replace established histopathological criteria, it may serve as a supportive pathological feature when interpreted alongside conventional morphological parameters. Standardization of mast cell detection and quantification methods, combined with immunohistochemical and molecular profiling, may enhance the diagnostic and prognostic utility of mast cells in uterine smooth muscle tumors.

Further large-scale, well-designed studies with clinicopathological correlation are required to clarify the precise role of mast cells in tumor progression and to determine their potential as adjunctive markers in routine gynecological pathology practice.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3004-3008 | ISSN:2251-6727

We are grateful to all the patients who participated in the research for their cooperation and trust. Special thanks to the medical and technical staff for their assistance in data collection and patient care. MCN: IU/R&D/2025-MCN0004185

EthicalStatement

This review article is based exclusively on the analysis and synthesis of previously published studies available in the public domain. No new human participants, animal subjects, or identifiable patient data were involved in the preparation of this manuscript. Therefore, approval from an institutional ethics committee or informed consent was not required.

Acknowledgment

The author sincerely acknowledges Dr. Nausheen Sanaullah Khan for her valuable guidance, constant support, and academic mentorship throughout the preparation of this review article. The author also extends gratitude to the faculty and staff of IIMSR for providing a supportive academic environment and access to necessary resources

ConflictOf Interest

The author declares that there are no conflicts of interest, financial or non-financial, related to the content of this review article

References

[1] Orii, A.; Mori, A.; Zhai, Y. L.; Toki, T.; Nikaido, T.; Fujii, S. Mast Cells in Smooth Muscle Tumors of the Uterus. Int. J. Gynecol. Pathol. 1998, 17(4), 336–342.

[2] Abeyratne, N. V. A.; Santos, L. D.; Yong, L. Y. C. Distribution of Mast Cells in Uterine Leiomyomas and Myometrium and Their Relationship to Morphology. Pathology 2015, 47(6), 522–528.

[3] Gousuddin, M.; Roohi, S.; Pattankar, V. L. Common Lesions of Uterus and Cervix with Mast Cell Profile. Asian Pac. J. Health Sci. 2015, 2(2), 64–68.

[4] Apurva, V.; Sharma, P. K.; Manchanda, G. S.; Sharma, V. K.; Sood, S.; Vats, S. Mast Cell Profile in Myometrial Lesions: A Study of 577 Cases. Indian J. Basic Appl. Med. Res. 2016, 5(2), 646–650.

[5] Erol, A. Y.; Tokyol, C.; Ozdemir, O.; Yilmazer, M.; Arioz, D. T.; Aktepe, F. The Role of Mast Cells and Angiogenesis in Benign and Malignant Neoplasms of the Uterus. Pathol. Res. Pract. 2011, 207(10), 618–622.

[6] Jiang, L.; Hua, Y.; Shen, Q.; Ding, S.; Jiang, W.; Zhang, W.; Zhu, X. Role of Mast Cells in Gynecological Neoplasms. Front. Biosci. (Landmark Ed.) 2013, 18, 773–781.

[7] Komi, D. E. A.; Redegeld, F. A. Role of Mast Cells in Shaping the Tumour Microenvironment. Clin. Rev. Allergy Immunol. 2020, 58(3), 313–325.

[8] Ribatti, D. Mast Cells, Angiogenesis, and Tumour Growth. Biochim. Biophys. Acta Mol. Basis Dis. 2012, 1822(1), 2–8.

[9] Dall'Asta, A.; Gizzo, S.; Musaro, A.; Quaranta, M.; Noventa, M.; Migliavacca, C.; Ancona, E.; Nardelli, G. B. Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP): A Comprehensive Analysis of Clinicopathological Features. Am. J. Surg. Pathol. 2014, 38(6), 835–842.

[10] Shobhitha, D.; Reddy, K. R.; Sireesha, G.; Sujatha, B. Distribution of Mast Cells in Uterine Leiomyoma and Adjacent Myometrium. Natl. J. Lab. Med. 2023, 12(4), PO21–PO24.

[11] Yang, Q.; Guo, X.; Zhao, Y.; Chen, L.; Wang, Y. Comprehensive Review of Uterine Leiomyosarcoma: Pathology, Molecular Features, and Therapeutic Advances. Cells 2024, 13(13), 1106.