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CHAPTER

2

Etiopathogenesis of Chronic Pelvic Pain

Asha Baxi, Dhaval A Baxi

INTRODUCTION

Chronic pelvic pain (CPP) represents one of the most challenging clinical conditions in modern medicine, affecting millions of women worldwide and imposing substantial personal and societal burdens.[1] The complexity of CPP stems from its multifactorial etiology, involving multiple organ systems and pathophysiological mechanisms that can perpetuate pain even after resolution of initial pathology.[2] Recent advances in understanding pain mechanisms, particularly central sensitization, have revolutionized our approach to diagnosis and treatment, emphasizing the need for comprehensive, multimodal care strategies.[3]

DEFINITION AND EPIDEMIOLOGY

Chronic pelvic pain is consistently defined across the literature as persistent, noncyclic pain perceived in structures related to the pelvis, lasting more than 6 months.[2] This definition excludes pain due exclusively to dysmenorrhea or dyspareunia, though these may coexist with CPP.[4] The European Association of Urology has developed a multidimensional classification system distinguishing between chronic primary pelvic pain (without identifiable pathology) and secondary pelvic pain (associated with underlying disease).[5]

PREVALENCE AND GLOBAL IMPACT

Population-based studies demonstrate significant variation in CPP prevalence, ranging from 4% to 26.6%, depending on study design and case definitions.[6] Most robust estimates suggest a prevalence of 14–16% among women of reproductive age.[7] A comprehensive systematic review found prevalence rates between 5.7% and 26.6% globally, with variations attributed to differences in diagnostic criteria and study methodologies.[6] The condition affects women across all age groups, with most population-based studies focusing on reproductive-aged women.[7]

Cross-cultural studies reveal consistent prevalence patterns, suggesting universal susceptibility to CPP regardless of geographic or ethnic factors.[8] However, significant gaps exist in epidemiological data from many countries

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and regions, highlighting the need for standardized international research approaches.[8]

ETIOPATHOGENESIS OF CHRONIC PELVIC PAIN

Systemic Causes

Chronic pelvic pain rarely results from a single pathologic process, instead representing a complex interplay of multiple systems **(Fig. 1)**. The most common etiologies include:

- *Gynecological causes:* Endometriosis remains the leading identifiable cause of CPP, responsible for chronic pain symptoms in more than half of histologically confirmed cases.[9] Other significant gynecologic contributors include adenomyosis, pelvic inflammatory disease, adhesions, ovarian cysts, and uterine fibroids.[10] Pelvic congestion syndrome with vascular entrapment of nerves has also been established to be a prevalent condition causing CPP **(Flowchart 1)**.
- *Urological conditions:* Interstitial cystitis/bladder pain syndrome, recurrent urinary tract infections, and urethral syndrome contribute significantly to CPP presentations.[11] These conditions frequently coexist with other pelvic pain syndromes, reflecting shared pathophysiological mechanisms.[12]
- *Gastrointestinal disorders:* Irritable bowel syndrome is present in a substantial proportion of CPP patients, with studies suggesting overlap rates exceeding 50% in some populations.[12] Inflammatory bowel disease and functional dyspepsia also contribute to the overall pain experience.[13]
- *Musculoskeletal components:* Pelvic floor myalgia, abdominal wall myofascial pain, and hip/lower back dysfunction are increasingly

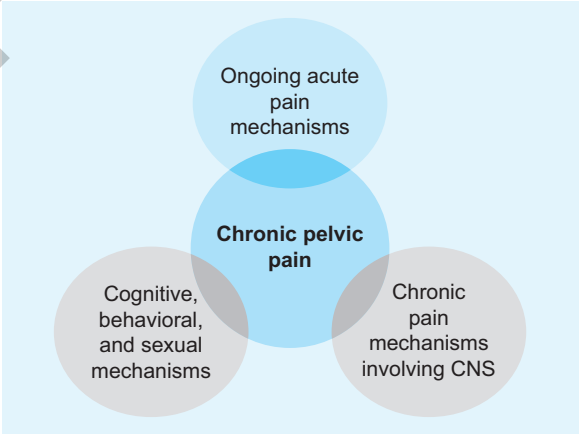
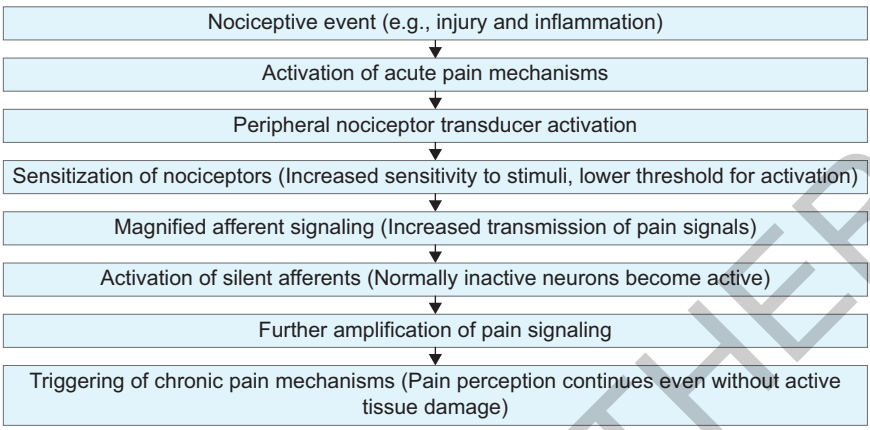


Fig. 1: Etiopathogenesis of chronic pelvic pain (CPP). (CNS: central nervous system)

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Flowchart 1: Possible signaling pathway from inflammation or injury to the pain perception.



recognized as primary or contributing factors in CPP. Studies using pressure algometry have demonstrated altered pain thresholds in pelvic floor muscles.[14]

CENTRAL SENSITIZATION AND NEUROPLASTICITY

Central sensitization has emerged as a fundamental mechanism underlying CPP persistence and progression.[15] This process involves increased membrane excitability and synaptic efficacy in the central nervous system, resulting in enhanced pain sensitivity even after peripheral pathology resolution.[15]

Key features of central sensitization in CPP include:

- *Hyperalgesia:* Decreased pain thresholds and amplified responses to nociceptive stimuli[16]
- *Allodynia:* Pain perception from normally nonpainful stimuli[16]
- *Temporal summation:* Increased pain perception with repeated stimulation[16]
- *Secondary hyperalgesia:* Spatial extension of pain beyond the original site[16]

Neuroimaging studies have identified structural and functional brain changes in CPP patients, including alterations in thalamic gray matter volume and functional connectivity patterns.[17] The Central Sensitization Inventory (CSI) has emerged as a valuable clinical tool for assessing centralized pain symptoms, with higher baseline scores predicting worse surgical outcomes in endometriosis patients.[18]

INFLAMMATORY MECHANISMS

Emerging evidence highlights the role of inflammatory cytokines in CPP pathogenesis and maintenance. Key inflammatory mediators include:

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- *Proinflammatory cytokines:* Elevated levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) are consistently found in women with endometriosis and other CPP conditions.[19] These markers correlate with pain severity and may serve as diagnostic biomarkers.[19]
- *Chemokines:* Monocyte chemotactic protein-1 (MCP1/CCL2) and macrophage inflammatory protein-1α (MIP1α/CCL3) are elevated in CPP patients and correlate with pain scores in some studies.[15] These chemokines facilitate immune cell recruitment and may contribute to neuroinflammation.[15]
- *Anti-inflammatory mediators:* IL-4 and IL-10 show altered patterns in CPP conditions, potentially reflecting compensatory mechanisms or disease-promoting activities.[20]

CLINICAL ASSESSMENT AND DIAGNOSIS

History and Physical Examination

Comprehensive evaluation of CPP requires systematic assessment of pain characteristics, associated symptoms, and functional impact. Critical elements include:[1]

- *Pain history:* Documentation of pain onset, duration, character (cramping, burning, electrical, or dull), temporal patterns, and relationship to menstrual cycle, urination, defecation, and sexual activity.[21]
- *Psychosocial assessment:* Screening for depression, anxiety, trauma history, and quality of life impacts is essential, as psychological comorbidities are significantly elevated in CPP patients.[22]
- *Physical examination:* Systematic evaluation should include abdominal, pelvic, and musculoskeletal assessment. Pelvic floor muscle evaluation for tenderness and hypertonicity is crucial.[23] Neuropelvic assessment may help in locating the dermatomes specific to neural source of pain.

Diagnostic Tools and Biomarkers

- *Imaging studies:* Transvaginal ultrasonography represents the first-line imaging modality. MRI is a valuable tool in the absence of an expert radiographer capable of identifying masses, cysts, and adenomyosis while detecting hydrosalpinx indicating possible pelvic inflammatory disease.[24] Doppler studies may help in detecting vascular compression of nerves.
- *Laboratory assessments:* While no definitive diagnostic biomarkers exist for idiopathic CPP, inflammatory markers show promise for specific conditions. IL-6 and TNF-α demonstrate significant elevation in endometriosis patients and correlate with disease severity.[25]
- *Specialized testing:* Quantitative sensory testing reveals altered pain processing in many CPP patients.[26]

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- *Validated Assessment Instruments for quantifying pain scores and their impact on day-to-day life of the patient include:* Pain Disability Index (PDI), CSI, Endometriosis Health Profile (EHP-30), Visual Analog Scale (VAS), and Numerical Rating Scale (NRS).[27]

CONCLUSION

Chronic pelvic pain is a multifactorial enigmatic clinical condition. Detailed attention should be given to the patients clinical history and symptoms since there may not be a single clear identifiable pathology in many cases. Such patients should be managed by a multidisciplinary team led by an experienced gynecologist with to help alleviate physical and psychological symptoms of such women. Breaking the cycle of pain is most important from the patients perspective along with finding the exact pathology to facilitate a permanent cure or long term relief.

Key Points

Chronic pelvic pain is a physically and mentally debilitating condition. A detailed history and evaluation with an empathetic approach is necessary to make an accurate diagnosis. In most conditions, it is possible to find the cause. In the absence of an obvious gynecological cause, interdisciplinary care may often help in diagnosing the condition and in guiding management. Understanding the neuroanatomy and specific pain therapy plays a vital role in managing these patients.

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