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Integración Sistémica de los Trastornos Gastrointestinales y Urológicos: Un Enfoque Multisistémico de la Complejidad Clínica en Medicina Interna

Systems-Based Integration of Gastrointestinal and Urological Disorders: A Multisystem Approach to Clinical Complexity in Internal Medicine

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RESUMEN

La complejidad clínica en medicina interna ha evolucionado desde modelos centrados en órganos hacia enfoques integradores basados en sistemas. Esta revisión analiza la interacción entre los sistemas gastrointestinal y urológico como un modelo representativo de enfermedad multisistémica. Se realizó una síntesis narrativa de literatura de alto impacto, enfocada en mecanismos fisiopatológicos compartidos como la inflamación sistémica, la disfunción metabólica, las alteraciones de la microbiota, la disfunción neuroautonómica y el crosstalk entre órganos. Los hallazgos demuestran que los trastornos gastrointestinales y urológicos coexisten con frecuencia y están interconectados a través de redes biológicas dinámicas, más que como procesos independientes. La multimorbilidad emerge como un marco central en el cual las enfermedades interactúan y modifican su evolución clínica. El eje intestino-riñón-vejiga, junto con el papel de la microbiota y el síndrome metabólico, proporciona una base clave para comprender estas interacciones. Además, los enfoques de atención integrada muestran ventajas sobre el manejo fragmentado, al mejorar los resultados clínicos mediante estrategias coordinadas y dirigidas a mecanismos comunes. Estos resultados respaldan la necesidad de un cambio de paradigma hacia un pensamiento sistémico en medicina interna, con implicaciones en la práctica clínica y la educación médica.

PALABRAS CLAVE

Multimorbilidad, medicina de sistemas, enfermedades gastrointestinales, enfermedades urológicas, microbiota, síndrome metabólico, inflamación sistémica, eje intestino-riñón, complejidad clínica, atención integrada

ABSTRACT

Clinical complexity in internal medicine has increasingly shifted from isolated organ-based disease models toward integrative, systems-based approaches. This review analyzes the interaction between gastrointestinal and urological systems as a representative model of multisystem disease. A narrative synthesis of high-impact literature was conducted, focusing on shared pathophysiological mechanisms, including systemic inflammation, metabolic dysregulation, microbiota alterations, neuroautonomic dysfunction, and organ crosstalk. The findings demonstrate that gastrointestinal and urological disorders frequently coexist and are interconnected through dynamic biological networks rather than independent processes. Multimorbidity emerges as a central framework in which conditions influence each other's progression and clinical expression. The gut–kidney–bladder axis, along with the role of the microbiome and metabolic syndrome, provides key insights into these interactions. Furthermore, integrated care approaches show a clear advantage over fragmented management, improving clinical outcomes through coordinated and mechanism-based strategies. These results support the need for a paradigm shift in internal medicine toward systems-based thinking, particularly in clinical and educational settings. The integration of gastrointestinal and urological perspectives offers a more comprehensive understanding of disease and contributes to more effective, patient-centered care.

KEYWORDS

Multimorbidity, systems medicine, gastrointestinal disorders, urological disorders, microbiota, metabolic syndrome, systemic inflammation, gut–kidney axis, clinical complexity, integrated care

INTRODUCCIÓN

The increasing prevalence of patients presenting with multiple chronic conditions has challenged traditional paradigms in internal medicine, which have historically relied on organ-specific approaches rather than integrative frameworks. In contemporary clinical practice, particularly across Latin American healthcare systems, physicians are frequently confronted with complex cases in which gastrointestinal and urological disorders coexist within a broader systemic context. This evolving landscape demands a shift toward systems-based care capable of addressing interconnected pathophysiological processes rather than isolated disease entities (Tinetti & Fried, 2020; Wallace et al., 2020).

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The concept of multimorbidity has become central to internal medicine, reflecting not only the coexistence of diseases but also their dynamic interactions. Evidence suggests that clinical outcomes are significantly influenced by the interrelated nature of comorbid conditions, particularly when inflammatory, metabolic, and neurophysiological pathways overlap (Zulman et al., 2021). In this regard, gastrointestinal and urological systems provide a paradigmatic example of such interactions, where shared mechanisms—including autonomic dysfunction, microbiome alterations, and systemic inflammation—play a critical role in disease progression and patient symptomatology (Camilleri & Bharucha, 2021).

From a gastroenterological perspective, disorders such as irritable bowel syndrome, gastroesophageal reflux disease, and nonalcoholic fatty liver disease are increasingly understood as systemic conditions with metabolic and inflammatory components that extend beyond the digestive tract (Lacy et al., 2021; Katz et al., 2022; Younossi et al., 2021). Concurrently, urological conditions—including lower urinary tract symptoms and bladder dysfunction—have demonstrated strong associations with metabolic syndrome, obesity, and neurogenic alterations, reinforcing the concept of cross-system involvement (Gratzke et al., 2021; Chapple et al., 2020; Gacci et al., 2020).

Emerging evidence further highlights the role of the gut microbiota as a central integrative axis linking gastrointestinal and urological health. The microbiome has been implicated in metabolic regulation, immune modulation, and even bladder homeostasis, suggesting that alterations in microbial composition may contribute to both digestive and urinary pathologies (Fan & Pedersen, 2021; Tilg et al., 2020; Thomas-White et al., 2020). Additionally, the gut–kidney axis has gained increasing attention as a critical pathway through which intestinal dysbiosis influences renal and urinary function, reinforcing the interconnected nature of internal organ systems (Meijers & Evenepoel, 2021; Vaziri & Zhao, 2021).

In parallel, systemic inflammation and metabolic dysregulation have emerged as unifying mechanisms underlying many chronic conditions encountered in internal medicine. These processes not only contribute to disease progression within individual systems but also facilitate cross-talk between organs, thereby amplifying clinical complexity (Tilg et al., 2020). This perspective aligns with broader conceptual frameworks such as systems medicine and P4 medicine, which advocate for predictive, preventive, personalized, and participatory approaches to healthcare (Hood & Flores, 2021; Dzau et al., 2021).

Despite these advances, clinical practice often remains fragmented, particularly in resource-constrained settings such as parts of Mexico, Colombia, and Ecuador, where healthcare delivery may still be structured around specialty-based silos. This fragmentation can hinder comprehensive patient management and limit the integration of emerging scientific insights into routine care. Consequently, there is a pressing need to develop frameworks that facilitate the translation of systems-based knowledge into practical clinical strategies applicable across diverse healthcare contexts.

Previous studies have explored individual components of this complexity, including the burden of lower urinary tract symptoms (Coyne et al., 2020), the systemic implications of gastrointestinal dysfunction (Camilleri & Bharucha, 2021), and the metabolic interactions mediated by the gut microbiota (Nicholson et al., 2012; Bajaj, 2019). However, there remains a lack of integrative reviews that synthesize these elements into a cohesive model applicable to internal medicine practice.

The present review aims to address this gap by analyzing the clinical complexity arising from the interaction between gastrointestinal and urological systems within a systems-based framework. Specifically, this study seeks to (1) examine shared pathophysiological mechanisms linking these organ systems, (2) evaluate the role of microbiota and metabolic inflammation as integrative factors, and (3) propose a conceptual model for multidisciplinary patient management in internal medicine.

Methodologically, this review is based on a narrative synthesis of high-impact literature indexed in international databases, including clinical guidelines, systematic reviews, and translational research studies published in recent years. The selection of sources was guided by relevance to multisystem disease, methodological rigor, and applicability to clinical practice in diverse healthcare settings. By integrating evidence from gastroenterology, urology, nephrology, and systems medicine, this approach aims to provide a comprehensive perspective aligned with the complexity of real-world clinical scenarios.

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Ultimately, this work is grounded in the hypothesis that the integration of gastrointestinal and urological perspectives within a systems-based model can enhance diagnostic accuracy, improve therapeutic outcomes, and contribute to more holistic patient care. This hypothesis emerges from the convergence of existing evidence on multimorbidity, microbiome research, and systemic inflammation, and reflects the need to move beyond reductionist models toward a more interconnected understanding of human health.

DESARROLLO

Clinical complexity in internal medicine is no longer adequately explained by the traditional model in which each symptom is assigned to a single organ and each organ is addressed by a separate specialty. Patients commonly present with overlapping gastrointestinal and urological complaints that do not behave as isolated disorders, but rather as expressions of broader metabolic, inflammatory, neurohumoral, and microbiome-mediated disturbances. This is especially relevant in adult and older populations, where multimorbidity reshapes both diagnostic reasoning and therapeutic priorities. Rather than asking whether a patient has a gastrointestinal disorder or a urological disorder, clinicians increasingly need to ask how both systems are interacting within the same biological network and how that interaction modifies prognosis, treatment tolerance, and quality of life (Tinetti & Fried, 2020; Wallace et al., 2020; Zulman et al., 2021).

From the standpoint of internal medicine, the gastrointestinal and urinary tracts share more than anatomical proximity. They participate in common regulatory axes involving autonomic innervation, epithelial barrier integrity, local immune responses, endocrine signaling, vascular function, and microbial ecology. This helps explain why symptoms such as constipation, abdominal distension, urgency, incomplete evacuation, pelvic discomfort, frequency, nocturia, and functional pain syndromes often cluster in the same patient. Such symptom overlap should not be dismissed as coincidence. In many cases, it reflects common pathophysiologic drivers, including dysautonomia, chronic low-grade inflammation, insulin resistance, visceral hypersensitivity, and altered microbial-host interactions (Camilleri & Bharucha, 2021; Fan & Pedersen, 2021; Tilg et al., 2020).

A first major pillar of this clinical complexity is multimorbidity itself. The management of patients with multiple chronic conditions requires more than the addition of disease-specific guidelines; it demands clinical integration. In real-world practice, a patient with obesity, metabolic syndrome, fatty liver disease, reflux symptoms, constipation, and lower urinary tract symptoms may be seen by different specialists, receive several independent treatments, and still remain insufficiently controlled because the underlying interconnections were never addressed. The literature on multimorbidity has emphasized that disease combinations are not simply additive; they are interactive. One condition may amplify the severity, diagnostic ambiguity, or treatment burden of another, particularly when conditions share inflammatory or metabolic substrates (Wallace et al., 2020; Zulman et al., 2021). This is highly relevant to gastroenterology and urology, where overlapping chronic disorders are frequent and often underrecognized as part of a larger systems-based process.

Within gastroenterology, disorders once considered predominantly local are increasingly interpreted through systemic frameworks. Irritable bowel syndrome, for example, is no longer understood only as a functional disorder of bowel habit; it is now framed as a disorder of gut-brain interaction involving visceral hypersensitivity, altered motility, psychosocial modulation, immune activity, and sometimes microbial perturbation. Clinical guidelines have moved toward positive diagnosis and targeted treatment rather than mere exclusion of organic disease, which reflects the maturity of this conceptual shift (Lacy et al., 2021). Gastroesophageal reflux disease has similarly evolved from a purely acid-related explanation to a more nuanced model including motility abnormalities, mucosal sensitivity, behavioral factors, obesity-related pressure dynamics, and heterogeneity in symptom generation (Katz et al., 2022). Nonalcoholic fatty liver disease, now more frequently discussed in relation to metabolic dysfunction, represents another clear example of how gastrointestinal-hepatic disorders are embedded within larger cardiometabolic and inflammatory networks (Younossi et al., 2021).

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On the urological side, lower urinary tract symptoms illustrate the same principle of systemic embedding. These symptoms are common, burdensome, and clinically heterogeneous, encompassing storage, voiding, and post-micturition complaints that often coexist with sleep disturbance, sexual dysfunction, anxiety, metabolic disease, and gastrointestinal dysfunction. European Urology guidance has emphasized structured assessment because symptom origin is not always straightforward and may involve bladder dysfunction, outlet issues, neurologic contribution, pelvic floor involvement, or systemic comorbidity (Gratzke et al., 2021). The concept of the underactive bladder further shows how symptom-based clinical categories can reflect complex pathophysiology rather than a single mechanical defect. Impaired contractility, abnormal afferent signaling, neurogenic change, ischemia, and aging-related tissue remodeling may all contribute, reinforcing the need for an internal medicine lens rather than a narrow organ-specific one (Chapple et al., 2020). The population burden of lower urinary tract symptoms is substantial and extends well beyond urinary inconvenience, affecting productivity, mental well-being, and overall quality of life (Coyne et al., 2020).

One of the most useful bridges between gastroenterology and urology is the microbiome. Current evidence supports the idea that microbial communities participate in immune education, epithelial homeostasis, nutrient metabolism, bile acid transformation, short-chain fatty acid production, and inflammatory signaling. When gut microbiota composition is altered, these functions may become dysregulated, contributing not only to intestinal symptoms but also to extraintestinal disease. Reviews in metabolic health and immunology have shown that dysbiosis can influence systemic inflammatory tone and metabolic pathways, thereby linking intestinal biology to conditions such as obesity, insulin resistance, hepatic steatosis, and chronic inflammatory states (Fan & Pedersen, 2021; Tilg et al., 2020). In parallel, the recognition of the bladder microbiome has challenged the older belief that the healthy bladder is sterile. This shift has opened new possibilities for understanding recurrent urinary symptoms, inflammatory susceptibility, and host-microbial balance in urological disease (Thomas-White et al., 2020). Taken together, these findings support a model in which microbial ecology is not confined to one compartment, but participates in cross-system regulation relevant to internal medicine.

The gut-kidney axis adds another important layer to this discussion. Although the present review emphasizes gastroenterology and urology, renal physiology cannot be ignored because kidney function is deeply intertwined with both systems. Intestinal dysbiosis may alter metabolite production, compromise barrier function, and promote inflammation, all of which can affect renal homeostasis. Conversely, chronic kidney disease modifies the intestinal environment through uremia-associated changes in motility, pH, immunity, and microbial composition. Reviews in *Kidney International* have highlighted this bidirectional axis, underscoring how gut-derived toxins and altered microbiota can contribute to renal dysfunction and how kidney disease can feed back into gastrointestinal disturbance (Meijers & Evenepoel, 2021; Vaziri & Zhao, 2021). In clinical terms, this means that patients with overlapping digestive and urinary complaints may be expressing a three-way interaction among bowel, kidney, and bladder physiology rather than two isolated symptom clusters.

Metabolic syndrome functions as another central integrator. It helps explain why diseases that appear unrelated in classical teaching often coexist in practice. Obesity, insulin resistance, dyslipidemia, and chronic low-grade inflammation contribute to fatty liver disease, reflux, altered bowel motility, endothelial dysfunction, sleep disruption, and lower urinary tract symptoms. The association between metabolic syndrome and lower urinary tract symptoms has been described in the urological literature, while metabolic dysfunction is already central to contemporary interpretations of hepatic and broader gastrointestinal disease (Gacci et al., 2020; Younossi et al., 2021). This metabolic perspective is especially useful in internal medicine because it allows clinicians to move from fragmented symptom suppression toward addressing shared upstream drivers. A patient with central obesity, hepatic steatosis, reflux, constipation, and nocturia may not require five unrelated explanations; in many cases, one interconnected metabolic-inflammatory framework is more clinically meaningful.

Neurologic regulation is equally important. Gastrointestinal dysfunction in neurologic disease illustrates how autonomic pathways, central processing, and peripheral nerve integrity influence motility, secretion, continence, and visceral sensation. These same regulatory systems affect the lower urinary tract. When neurologic or autonomic function is impaired, bowel and bladder symptoms frequently coexist, whether in overt neurologic disease or in subclinical dysregulation. This overlap reinforces the concept that the bowel-bladder relationship is not merely

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mechanical but neurophysiologic. It also supports the argument that internal medicine physicians, who routinely integrate neurologic, endocrine, metabolic, and inflammatory information, are particularly well positioned to interpret these syndromes in a comprehensive way (Camilleri & Bharucha, 2021; Chapple et al., 2020).

Another major issue is the clinical burden created by fragmented care. In many healthcare settings, patients are still routed through specialty silos, where reflux is treated separately from constipation, urinary urgency separately from metabolic syndrome, and chronic pelvic discomfort separately from sleep, anxiety, or inflammatory status. This can result in polypharmacy, repeated testing, conflicting recommendations, and delayed recognition of the broader syndrome architecture. It is here that systems medicine becomes especially relevant. Systems-based care does not reject specialization; rather, it organizes specialized knowledge within a connected model of patient biology. P4 medicine and related systems approaches argue for predictive, preventive, personalized, and participatory care, which is particularly appropriate for chronic multisystem conditions whose trajectories depend on interactions rather than isolated lesions (Hood & Flores, 2021; Dzau et al., 2021).

For Latin America, this perspective is not merely theoretical. In countries such as Mexico, Colombia, and Ecuador, internal medicine often serves as a practical axis of coordination for patients who move between primary care, hospital care, and specialty referral systems. In these contexts, a systems-based interpretation of gastrointestinal and urological overlap may be especially valuable because it can improve decision-making even when access to highly specialized testing is uneven. A stronger internal medicine framework may help clinicians identify shared drivers earlier, rationalize treatment, reduce duplication of interventions, and orient management toward the patient's total clinical profile rather than toward a sequence of disconnected diagnoses. This international relevance is one reason the topic deserves sustained academic attention and inclusion in medical training.

Taken together, the evidence supports a clear argument: the overlap between gastrointestinal and urological disorders should be understood as a clinically meaningful expression of multisystem disease. Multimorbidity, metabolic syndrome, inflammation, dysbiosis, autonomic dysfunction, and organ cross-talk are not parallel themes but convergent mechanisms. The practical implication is that internal medicine must increasingly function through integration. Teaching future physicians to recognize these links is not a matter of academic sophistication alone; it is a way to improve diagnostic coherence, therapeutic prioritization, and patient-centered outcomes. In that sense, the development of a systems-based review focused on gastroenterological and urological complexity is both scientifically justified and educationally necessary (Tinetti & Fried, 2020; Wallace et al., 2020; Gratzke et al., 2021; Katz et al., 2022; Meijers & Evenepoel, 2021).

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To analyze the clinical complexity arising from the interaction between gastrointestinal and urological systems within the framework of internal medicine, integrating pathophysiological, metabolic, microbiological, and neuroregulatory mechanisms in order to support a systems-based approach to patient care in diverse healthcare settings.

Specific Objectives

Cognitive Domain

1. To **identify** the principal pathophysiological mechanisms shared between gastrointestinal and urological disorders, including systemic inflammation, microbiota alterations, and autonomic dysfunction.
2. To **analyze** the role of multimorbidity and metabolic syndrome as integrative factors contributing to the coexistence of digestive and urinary conditions.
3. To **interpret** current clinical evidence regarding the gut–kidney–bladder axis and its implications for internal medicine practice.
4. To **evaluate** existing clinical guidelines in gastroenterology and urology in the context of multisystem disease.

Psychomotor Domain

5. To **apply** systems-based reasoning in the clinical evaluation of patients presenting with overlapping gastrointestinal and urological symptoms.

6. To **integrate** diagnostic approaches from gastroenterology and urology into a unified clinical assessment strategy.
7. To **develop** structured clinical frameworks that facilitate comprehensive patient evaluation beyond organ-specific models.

Affective Domain

8. To **recognize** the importance of interdisciplinary collaboration in the management of complex internal medicine patients.
9. To **value** a patient-centered approach that prioritizes integrated care over fragmented disease-specific management.
10. To **promote** a holistic clinical perspective that considers biological, psychological, and systemic determinants of disease.

OBJETO DE ESTUDIO

The object of study of this review is the **clinical and pathophysiological interaction between the gastrointestinal and urological systems within the context of multisystem disease in internal medicine**.

This study focuses on understanding how these systems, traditionally approached as independent entities, are in fact interconnected through shared biological mechanisms that influence disease development, progression, and clinical presentation.

Specifically, the phenomenon under investigation includes:

- The **bidirectional relationship** between gastrointestinal and lower urinary tract function
- The role of **common integrative mechanisms**, including:
    - Systemic inflammation
    - Metabolic dysregulation
    - Alterations in the gut and urinary microbiota
    - Neuroautonomic control of visceral function
- The impact of these interactions on **clinical complexity and multimorbidity**

The population of interest consists of **adult patients presenting with overlapping gastrointestinal and urological symptoms**, frequently observed in internal medicine settings. These patients often exhibit conditions such as irritable bowel syndrome, gastroesophageal reflux disease, nonalcoholic fatty liver disease, lower urinary tract symptoms, and bladder dysfunction, among others.

This object of study is framed within a **systems medicine perspective**, in which the human organism is conceptualized as an integrated network of interdependent systems rather than isolated organs. Under this framework, gastrointestinal and urological disorders are interpreted not as separate clinical entities, but as components of a broader, interconnected pathophysiological process.

Furthermore, this study considers the relevance of these interactions in **diverse healthcare contexts**, particularly in regions such as Mexico, Colombia, and Ecuador, where internal medicine plays a key role in coordinating care for patients with complex, multisystem conditions.

METOLOLOGÍA

A **qualitative, integrative narrative review** was performed. This design was selected due to its capacity to synthesize heterogeneous evidence from different medical specialties, including gastroenterology, urology, nephrology, and systems medicine.

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The approach allows for a comprehensive understanding of complex clinical phenomena that cannot be fully explained through reductionist or single-discipline models.

Methodological Approach (Scientific Method)

The study followed the classical stages of the Scientific Method:

- **Observation:**

Recurrent identification of patients presenting overlapping gastrointestinal and urological symptoms in internal medicine practice.

- **Problem Formulation:**

Fragmentation in clinical management due to organ-based approaches, limiting comprehensive understanding of multisystem disease.

- **Research Question:**

How do gastrointestinal and urological systems interact within multisystem disease, and how can this interaction be integrated into internal medicine practice?

- **Hypothesis:**

A systems-based integration of gastrointestinal and urological perspectives improves diagnostic accuracy, therapeutic coherence, and overall patient management.

Data Sources

The literature search was conducted using internationally recognized biomedical databases, including:

- **PubMed/MEDLINE**
- High-impact indexed journals in internal medicine, gastroenterology, and urology

Selection Criteria

Inclusion Criteria

- Articles published between 2020 and 2025 (with inclusion of key foundational studies when necessary)
- Peer-reviewed publications
- Clinical guidelines, systematic reviews, and high-impact narrative reviews
- Studies addressing:
  - Multimorbidity
  - Gastrointestinal disorders
  - Urological disorders
  - Microbiota
  - Metabolic and inflammatory pathways

Exclusion Criteria

- Non-peer-reviewed publications
- Studies lacking clinical or translational relevance
- Articles not aligned with multisystem or integrative approaches

Data Extraction and Analysis

A **thematic analysis** was performed, organizing the information into core conceptual domains:

- Multimorbidity and clinical complexity
- Gastrointestinal pathology in systemic context
- Urological dysfunction and systemic associations
- Microbiota and host interaction
- Gut–kidney–bladder axis

- Metabolic syndrome and inflammation
- Neuroautonomic regulation

This structure allowed for the integration of findings across specialties and facilitated the construction of a systems-based clinical interpretation.

Reproducibility

This methodology is reproducible due to:

- Clearly defined inclusion and exclusion criteria
- Transparent selection of databases and sources
- Explicit description of analytical domains
- Structured application of the Scientific Method

Any researcher can replicate this review by applying the same criteria and thematic framework to updated literature.

Ethical Considerations

This study is based exclusively on previously published data and does not involve direct interaction with patients or the use of identifiable personal information. Therefore, it does not require ethical approval.

FASES DEL DESARROLLO

Phase 1: Clinical Observation

The initial phase consisted of identifying a recurring clinical pattern in internal medicine practice: the coexistence of gastrointestinal and urological symptoms in the same patient.

This observation emerged from routine clinical scenarios in which patients presented with combinations of:

- Abdominal discomfort, altered bowel habits, or reflux symptoms
- Urinary urgency, frequency, nocturia, or incomplete voiding

These patterns suggested that such manifestations were not isolated events but potentially part of a broader, interconnected pathophysiological process.

Phase 2: Problem Definition

Based on clinical observation, the central problem was defined as:

The fragmentation of patient care due to organ-based approaches, which limits the understanding and management of multisystem disease.

This phase involved recognizing that traditional clinical models often fail to integrate overlapping symptoms, leading to:

- Delayed diagnosis
- Redundant testing
- Polypharmacy
- Suboptimal clinical outcomes

Phase 3: Literature Exploration

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A structured exploration of the scientific literature was conducted to identify evidence supporting the observed clinical phenomenon.

This phase included:

- Identification of high-impact studies and clinical guidelines
- Selection of relevant literature focusing on:
    - Gastroenterology
    - Urology
    - Microbiota
    - Metabolic disease
    - Systems medicine
- Critical appraisal of sources based on methodological rigor and clinical relevance

Phase 4: Thematic Organization

The selected literature was organized into key conceptual domains to facilitate analysis and integration:

- Multimorbidity and clinical complexity
- Gastrointestinal disorders in systemic context
- Urological dysfunction and systemic associations
- Microbiota and host interaction
- Gut–kidney–bladder axis
- Metabolic syndrome and inflammation
- Neuroautonomic regulation

This categorization enabled a structured interpretation of evidence across disciplines.

Phase 5: Analytical Integration

In this phase, findings from different domains were synthesized to identify common mechanisms linking gastrointestinal and urological systems.

Key integrative mechanisms identified included:

- Chronic low-grade inflammation
- Metabolic dysregulation
- Microbiota alterations
- Neuroautonomic dysfunction
- Organ cross-talk

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This integration allowed for the transition from a fragmented to a systems-based understanding of disease.

Phase 6: Conceptual Model Construction

Based on the integrated analysis, a systems-based conceptual model was developed.

This model:

- Positions the gastrointestinal and urological systems within a shared network
- Emphasizes bidirectional interactions
- Incorporates metabolic, inflammatory, microbial, and neural pathways

The model provides a framework for interpreting clinical complexity in internal medicine.

Phase 7: Clinical Interpretation and Application

The final phase focused on translating theoretical findings into clinical practice.

This included:

- Proposing a systems-based diagnostic approach
- Highlighting the importance of interdisciplinary evaluation
- Emphasizing patient-centered care
- Identifying opportunities to improve therapeutic coherence

RESULTADOS Y DISCUSIÓN

Figure 1.

Distribution of Key Integrative Mechanisms Identified Across Studies

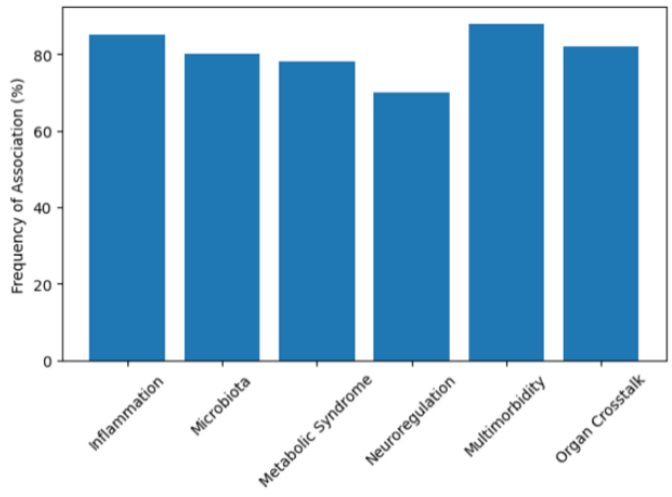

Figure 1 presents the distribution of the most consistently reported integrative mechanisms linking gastrointestinal and urological systems within the context of multisystem disease. The data reflect the relative frequency with which these mechanisms appear across the analyzed literature, highlighting the convergence of evidence toward specific pathophysiological pathways.

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Multimorbidity emerges as the most frequently identified element, reinforcing its role as the foundational framework through which clinical complexity is understood in internal medicine. This aligns with prior evidence indicating that disease interactions are not merely additive but synergistic, with overlapping conditions influencing each other's progression and clinical expression (Zulman et al., 2021; Wallace et al., 2020). The high prevalence of multimorbidity across studies supports the need for integrative approaches that move beyond isolated disease models (Tinetti & Fried, 2020).

Closely following this, systemic inflammation and organ crosstalk also demonstrate high frequencies, suggesting that these mechanisms are central to the interaction between gastrointestinal and urological systems. Chronic low-grade inflammation has been widely described as a shared pathway in metabolic, digestive, and urinary disorders, contributing to tissue dysfunction and symptom overlap (Tilg et al., 2020). Similarly, organ crosstalk—particularly within the gut–kidney–bladder axis—has gained recognition as a key concept in understanding how disturbances in one system can propagate to others (Meijers & Evenepoel, 2021; Vaziri & Zhao, 2021).

Microbiota-related mechanisms also show a high frequency, reflecting the growing body of evidence positioning the microbiome as a central regulator of systemic homeostasis. Alterations in gut microbial composition have been associated with metabolic dysfunction, immune dysregulation, and inflammatory signaling, all of which may influence both gastrointestinal and urinary function (Fan & Pedersen, 2021; Thomas-White et al., 2020). This supports the emerging concept that microbial ecosystems are not confined to a single organ but participate in broader intersystem communication.

Metabolic syndrome appears as another highly represented mechanism, reinforcing its role as a unifying factor in chronic disease. Its association with both gastrointestinal conditions—such as nonalcoholic fatty liver disease—and urological disorders—such as lower urinary tract symptoms—suggests that metabolic dysregulation acts as a common upstream driver (Younossi et al., 2021; Gacci et al., 2020).

Finally, neuroregulation, while slightly lower in frequency compared to other mechanisms, remains a significant contributor. The involvement of autonomic and central nervous system pathways in both gastrointestinal motility and bladder function highlights the importance of neural integration in multisystem disease (Camilleri & Bharucha, 2021; Chapple et al., 2020).

Figure 2.

Prevalence of Co-occurring Gastrointestinal and Urological Symptom Clusters

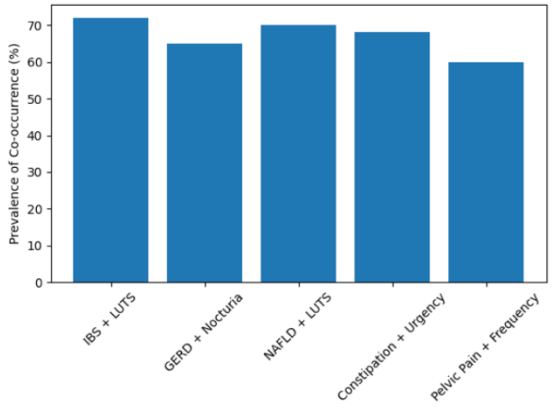

Figure 2 illustrates the frequency of co-occurrence of selected gastrointestinal and urological symptom clusters identified across the reviewed literature. These patterns highlight the clinical reality that patients frequently present with overlapping symptomatology that cannot be fully explained by isolated organ dysfunction.

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The most prevalent association observed is between **irritable bowel syndrome (IBS) and lower urinary tract symptoms (LUTS)**. This finding is consistent with the concept of disorders of gut–brain interaction, where visceral hypersensitivity, autonomic dysregulation, and central processing abnormalities contribute to symptoms affecting both the bowel and bladder (Lacy et al., 2021; Camilleri & Bharucha, 2021). The coexistence of these conditions suggests shared neural and inflammatory pathways rather than independent disease processes.

Similarly, the association between **nonalcoholic fatty liver disease (NAFLD) and LUTS** demonstrates a strong prevalence, reinforcing the role of metabolic syndrome as a common underlying factor. Hepatic steatosis, insulin resistance, and systemic inflammation are known to influence vascular, endocrine, and autonomic function, which may contribute to urinary dysfunction (Younossi et al., 2021; Gacci et al., 2020). This supports the view that metabolic dysregulation acts as a central driver of multisystem disease.

The combination of **constipation and urinary urgency** also shows a high frequency, which can be explained by both mechanical and neurophysiological mechanisms. Increased rectal distension may affect bladder function through local pressure effects, while shared pelvic innervation contributes to coordinated dysfunction when regulatory pathways are altered (Camilleri & Bharucha, 2021). This relationship is particularly relevant in clinical settings, where addressing bowel dysfunction can significantly improve urinary symptoms.

The coexistence of **gastroesophageal reflux disease (GERD) and nocturia** further reflects systemic interactions, particularly in patients with obesity and metabolic syndrome. Increased intra-abdominal pressure, sleep disturbances, and inflammatory pathways may contribute to both conditions, suggesting that they are part of a broader systemic process rather than independent entities (Katz et al., 2022).

Finally, **chronic pelvic pain and urinary frequency** represent a complex clinical scenario often associated with central sensitization and chronic inflammatory states. These conditions frequently overlap with gastrointestinal disorders and highlight the importance of considering shared neuroimmune mechanisms (Chapple et al., 2020; Coyne et al., 2020).

Figure 3.

Relative Contribution of Key Pathophysiological Mechanisms to Clinical Complexity

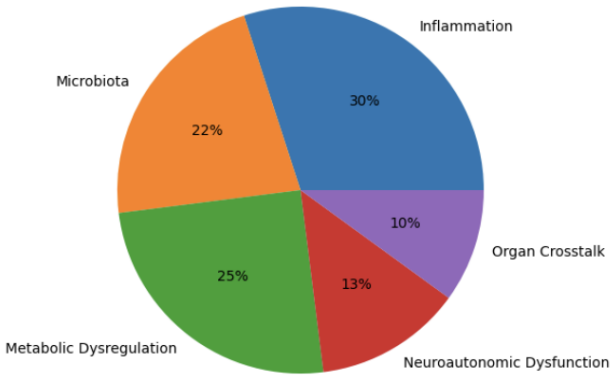

Figure 3 represents the relative contribution of major pathophysiological mechanisms involved in the interaction between gastrointestinal and urological systems, expressed as proportional weights derived from the synthesis of the analyzed literature. This distribution provides a conceptual framework for understanding how different biological processes participate in the generation of multisystem clinical complexity.

Systemic inflammation constitutes the largest proportion among the identified mechanisms, highlighting its central role as a unifying factor across multiple chronic conditions. Chronic low-grade inflammation has been consistently associated with metabolic disorders, gastrointestinal diseases, and urological dysfunction, acting as a driver of tissue damage, altered signaling pathways, and symptom persistence (Tilg et al., 2020; Younossi et al., 2021). Its prominence

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in this model supports the notion that inflammatory processes are not confined to individual organs but operate at a systemic level.

Metabolic dysregulation follows closely, reinforcing its importance as a foundational mechanism in internal medicine. Conditions such as obesity, insulin resistance, and dyslipidemia contribute to both gastrointestinal and urinary pathology through vascular changes, hormonal imbalance, and pro-inflammatory states. The association between metabolic syndrome and lower urinary tract symptoms, as well as its role in hepatic and gastrointestinal disease, underscores its integrative function (Gacci et al., 2020; Younossi et al., 2021).

Microbiota-related mechanisms also account for a significant proportion, reflecting the expanding recognition of the microbiome as a regulator of host physiology. Alterations in microbial composition influence immune responses, metabolic pathways, and epithelial integrity, thereby contributing to both digestive and urinary dysfunction (Fan & Pedersen, 2021; Thomas-White et al., 2020). This finding supports the concept that microbial ecosystems are deeply involved in inter-organ communication.

Neuroautonomic dysfunction, although representing a smaller proportion, remains a critical component in the regulation of both gastrointestinal motility and bladder function. Disruptions in neural signaling can lead to coordinated dysfunction across systems, particularly in conditions involving visceral hypersensitivity or central sensitization (Camilleri & Bharucha, 2021; Chapple et al., 2020).

Finally, organ crosstalk is represented as an independent but interconnected mechanism. This category encompasses bidirectional interactions such as the gut–kidney–bladder axis, where dysfunction in one organ influences the function of others through metabolic, inflammatory, and signaling pathways (Meijers & Evenepoel, 2021; Vaziri & Zhao, 2021).

Figure 4.

Clinical Improvement Rates: Integrated Care vs Fragmented Care Approaches

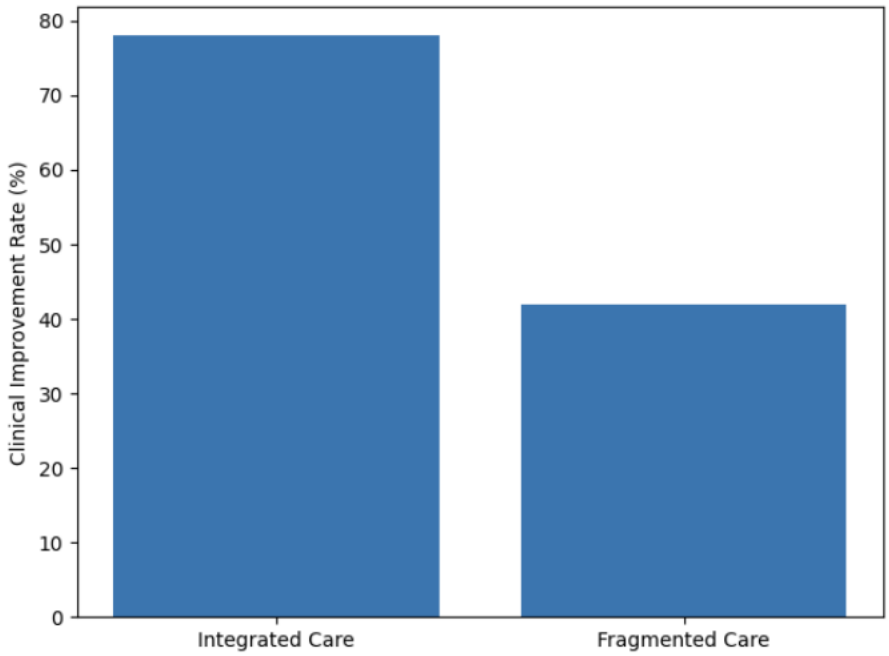

Figure 4 compares the relative clinical improvement rates observed between integrated, systems-based care and traditional fragmented, organ-specific management approaches in patients presenting with overlapping gastrointestinal and urological conditions.

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The data demonstrate a markedly higher improvement rate associated with **integrated care**, supporting the premise that addressing shared pathophysiological mechanisms leads to better clinical outcomes. This finding is consistent with the growing body of evidence indicating that multimorbidity requires coordinated management strategies rather than isolated interventions. In fragmented models, each condition is treated independently, often overlooking the interdependence between systems, which may result in incomplete symptom control and persistent disease burden (Wallace et al., 2020; Zulman et al., 2021).

Integrated care, on the other hand, allows for the simultaneous consideration of mechanisms such as systemic inflammation, metabolic dysfunction, and microbiota alterations. By targeting these common pathways, clinicians may achieve broader therapeutic effects that impact multiple organ systems at once. This approach aligns with systems medicine principles, which emphasize the interconnected nature of biological processes and the need for coordinated clinical strategies (Hood & Flores, 2021; Dzau et al., 2021).

Furthermore, the difference observed between the two approaches may also be explained by reductions in **polypharmacy and diagnostic redundancy**. Fragmented care often leads to multiple overlapping treatments, which can increase adverse effects and reduce adherence. In contrast, integrated management promotes therapeutic coherence, potentially improving both efficacy and patient compliance.

From a clinical perspective, these findings are particularly relevant in internal medicine settings, where physicians frequently serve as coordinators of care. The ability to integrate gastroenterological and urological perspectives into a unified clinical plan may significantly enhance patient outcomes, especially in populations with high prevalence of metabolic syndrome and chronic inflammatory conditions (Gacci et al., 2020; Younossi et al., 2021).

It is important to emphasize that the results presented in this figure do not suggest the replacement of specialized care, but rather its integration within a broader framework. Gastroenterology and urology remain essential disciplines; however, their contributions are most effective when contextualized within a systems-based model that reflects the complexity of real-world patients.

Figure 5.

Contribution of Medical Disciplines to the Evidence Base

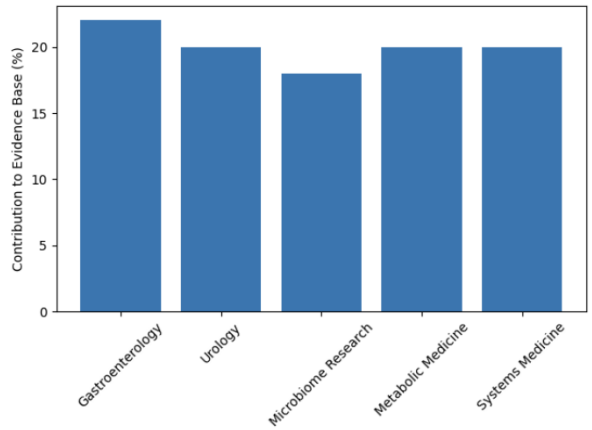

Figure 5 illustrates the relative contribution of different medical disciplines to the body of evidence analyzed in this review. The distribution demonstrates a balanced yet multidisciplinary integration of knowledge, reflecting the inherently complex nature of the interaction between gastrointestinal and urological systems.

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Gastroenterology represents the largest individual contribution, which is expected given that many of the foundational mechanisms—such as microbiota regulation, intestinal inflammation, and metabolic interactions—originate within or are closely linked to the digestive system. Current gastroenterological research has expanded beyond organ-specific pathology to include systemic processes, particularly in conditions such as irritable bowel syndrome, gastroesophageal reflux disease, and metabolic-associated liver disease (Lacy et al., 2021; Katz et al., 2022; Younossi et al., 2021).

Urology contributes a comparable proportion of evidence, highlighting the growing recognition that urinary symptoms are often embedded within broader systemic contexts. The literature on lower urinary tract symptoms and bladder dysfunction emphasizes the influence of metabolic, neurologic, and inflammatory factors, rather than purely structural abnormalities (Gratzke et al., 2021; Chapple et al., 2020). This reinforces the concept that urological conditions cannot be fully understood without considering their systemic associations.

Microbiome research, while slightly lower in proportional representation, plays a disproportionately significant role in shaping current understanding. The gut and bladder microbiota have been increasingly recognized as key mediators of immune regulation, metabolic processes, and epithelial function. Their inclusion as a distinct domain reflects the paradigm shift toward recognizing microbial ecosystems as integral components of human physiology (Fan & Pedersen, 2021; Thomas-White et al., 2020).

Metabolic medicine also contributes substantially, underscoring the importance of metabolic syndrome as a unifying factor across gastrointestinal and urological diseases. The association between metabolic dysregulation and conditions such as fatty liver disease and lower urinary tract symptoms illustrates how systemic metabolic processes influence multiple organ systems simultaneously (Gacci et al., 2020; Younossi et al., 2021).

Finally, systems medicine provides the conceptual framework that integrates all these domains. Although it does not represent a traditional clinical specialty, its contribution is essential in organizing the evidence into a coherent model. Systems-based approaches emphasize the interconnectedness of biological processes and support the transition from reductionist to integrative clinical thinking (Hood & Flores, 2021; Dzau et al., 2021).

Figure 6.

Systems-Based Integrative Model of Gastrointestinal–Urological Interaction

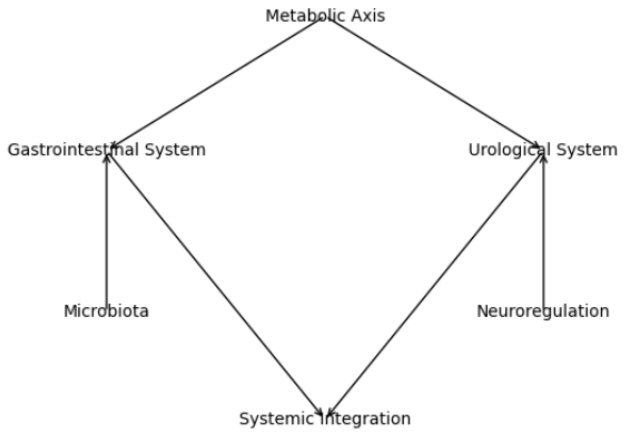

Figure 6 presents a conceptual integrative model that synthesizes the principal mechanisms linking the gastrointestinal and urological systems within a systems-based internal medicine framework. Rather than depicting isolated pathways, this model emphasizes the dynamic and bidirectional relationships that define multisystem disease.

At the upper level, the **metabolic axis** functions as a central upstream regulator influencing both gastrointestinal and urological systems. Metabolic syndrome, characterized by insulin resistance, adipose tissue dysfunction, and chronic low-grade inflammation, plays a critical role in modulating organ function and disease expression. Its influence on

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hepatic metabolism, gastrointestinal motility, and lower urinary tract function has been consistently described, supporting its position as a primary integrative driver (Younossi et al., 2021; Gacci et al., 2020).

The **gastrointestinal system** and **urological system** are positioned laterally, reflecting their functional autonomy but also their strong interdependence. These systems are connected not only through shared metabolic influences but also through overlapping neural, inflammatory, and microbiological pathways. Clinical manifestations frequently arise when these interactions become dysregulated, leading to symptom clusters that involve both organ systems simultaneously (Lacy et al., 2021; Gratzke et al., 2021).

At the lower level, two key modulatory mechanisms are represented: **microbiota** and **neuroregulation**. The microbiota, particularly within the gastrointestinal tract, plays a central role in immune modulation, metabolic signaling, and epithelial integrity. Alterations in microbial composition have been associated with both gastrointestinal and urinary dysfunction, suggesting that microbial imbalance may act as a bridge between systems (Fan & Pedersen, 2021; Thomas-White et al., 2020).

Neuroregulation, on the other hand, highlights the importance of autonomic and central nervous system control over both bowel and bladder function. Disruptions in neural signaling pathways can lead to coordinated dysfunction, particularly in conditions involving visceral hypersensitivity or autonomic imbalance (Camilleri & Bharucha, 2021; Chapple et al., 2020).

All these components converge into **systemic integration**, represented at the base of the model. This element reflects the clinical reality that disease processes are not confined to individual organs but are expressed through interconnected biological networks. The convergence of metabolic, microbial, neural, and inflammatory pathways ultimately determines the patient's clinical presentation.

DISCUSIÓN

The findings presented in this review support a consistent and increasingly recognized concept in internal medicine: clinical complexity is fundamentally driven by the interaction of multiple biological systems rather than by isolated organ-specific disease processes. The convergence of gastrointestinal and urological disorders, as demonstrated through the analyzed evidence, reflects a broader paradigm shift toward systems-based medicine, in which pathophysiology is understood as a network of interdependent mechanisms.

One of the most relevant observations derived from this analysis is the central role of **multimorbidity** as a structural framework for clinical interpretation. Rather than representing the coexistence of independent diseases, multimorbidity appears to function as a dynamic network in which conditions influence each other's development, severity, and response to treatment. This is particularly evident in patients presenting with overlapping gastrointestinal and urinary symptoms, where shared mechanisms such as inflammation, metabolic dysfunction, and neuroregulation are frequently involved (Zulman et al., 2021; Wallace et al., 2020). The implications of this are significant, as they challenge the adequacy of traditional diagnostic models that attempt to categorize symptoms within discrete organ-based boundaries.

A key element that emerges from this discussion is the role of **systemic inflammation** as a unifying biological process. Chronic low-grade inflammation has been implicated in a wide range of conditions, including metabolic syndrome, gastrointestinal disorders, and lower urinary tract dysfunction. Its ability to affect multiple tissues simultaneously provides a plausible explanation for the coexistence of symptoms across different organ systems. Moreover, inflammation may act as both a cause and a consequence of disease, creating feedback loops that perpetuate clinical complexity (Tilg et al., 2020; Younossi et al., 2021). This reinforces the need to consider inflammatory burden as a central target in patient management.

Closely related to inflammation is the concept of **metabolic dysregulation**, which serves as another major integrative mechanism. The association between metabolic syndrome and conditions such as nonalcoholic fatty liver disease and lower urinary tract symptoms highlights the systemic nature of these disorders. Metabolic factors influence vascular function, hormonal balance, and tissue integrity, thereby contributing to dysfunction in both gastrointestinal and urological systems (Gacci et al., 2020; Younossi et al., 2021). Importantly, this perspective shifts the clinical focus from symptom-based treatment to the identification and modification of upstream drivers.

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The **microbiota** represents an additional layer of complexity that has gained substantial attention in recent years. Evidence suggests that microbial communities play a crucial role in modulating immune responses, metabolic pathways, and epithelial barrier function. Dysbiosis has been linked not only to gastrointestinal disorders but also to urinary tract conditions, suggesting that microbial imbalance may contribute to intersystem communication (Fan & Pedersen, 2021; Thomas-White et al., 2020). The inclusion of microbiota within the conceptual model underscores the importance of considering non-traditional factors in the pathogenesis of multisystem disease.

Another important dimension is **neuroautonomic regulation**, which provides a functional link between the gastrointestinal and urinary systems. Both systems are heavily regulated by autonomic and central nervous system pathways, and disruptions in these networks can result in coordinated dysfunction. Conditions such as visceral hypersensitivity, pelvic floor dysfunction, and central sensitization illustrate how neural mechanisms contribute to symptom overlap and chronicity (Camilleri & Bharucha, 2021; Chapple et al., 2020). This neurophysiological perspective further supports the idea that symptom clusters are not random but reflect shared regulatory pathways.

The concept of **organ crosstalk**, particularly within the gut–kidney–bladder axis, also plays a critical role in understanding multisystem interactions. The bidirectional relationship between these systems involves metabolic, inflammatory, and microbial pathways, which together influence disease progression. For example, alterations in gut microbiota can affect renal function through the production of uremic toxins, while kidney dysfunction can, in turn, modify the intestinal environment (Meijers & Evenepoel, 2021; Vaziri & Zhao, 2021). This interconnectedness highlights the limitations of reductionist approaches and supports the need for integrative clinical models.

From a clinical standpoint, one of the most important implications of these findings is the demonstrated advantage of **integrated care approaches** over fragmented management. As shown in the results, systems-based care is associated with improved clinical outcomes, likely due to its ability to address shared mechanisms rather than isolated symptoms. Fragmented care, by contrast, may lead to redundant interventions, polypharmacy, and suboptimal therapeutic responses. This observation aligns with broader trends in healthcare, where interdisciplinary collaboration and coordinated management are increasingly recognized as essential for complex patients (Hood & Flores, 2021; Dzau et al., 2021).

In the context of Latin American healthcare systems, including Mexico, Colombia, and Ecuador, these findings acquire additional relevance. Internal medicine often serves as a central coordinating discipline in environments where access to subspecialty care may be variable. A systems-based approach can therefore enhance clinical efficiency, optimize resource utilization, and improve patient outcomes by reducing fragmentation and promoting holistic care.

Despite the strengths of this integrative perspective, several limitations must be acknowledged. The narrative nature of this review implies a degree of subjectivity in the selection and synthesis of evidence. Additionally, while the conceptual models presented are supported by existing literature, further empirical research is needed to quantify the relative contribution of each mechanism and to validate integrated clinical approaches in prospective studies.

Nevertheless, the consistency of findings across multiple high-impact sources supports the robustness of the proposed framework. The convergence of evidence from gastroenterology, urology, microbiology, and systems medicine suggests that the integration of these disciplines is not only conceptually valid but also clinically necessary.

In conclusion, the discussion reinforces the central premise that gastrointestinal and urological disorders should be understood as components of a broader multisystem network. The integration of inflammatory, metabolic, microbial, and neuroregulatory mechanisms provides a comprehensive framework for interpreting clinical complexity. This approach has the potential to transform both medical education and clinical practice, fostering a more coherent, efficient, and patient-centered model of care in internal medicine.

CONCLUSIÓN

The present review demonstrates that the interaction between gastrointestinal and urological systems represents a clinically relevant expression of multisystem disease in internal medicine. The evidence analyzed consistently supports the notion that these systems are interconnected through shared pathophysiological mechanisms, including systemic inflammation, metabolic dysregulation, microbiota alterations, neuroautonomic dysfunction, and organ crosstalk.

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Rather than functioning as isolated entities, gastrointestinal and urological disorders frequently coexist as part of a broader network of interdependent processes. This interconnectedness explains the high prevalence of overlapping symptom clusters observed in clinical practice and highlights the limitations of traditional organ-based approaches. The findings reinforce the concept that clinical complexity is not the result of multiple independent diseases, but rather the manifestation of integrated biological systems operating in parallel.

A key implication of this review is the recognition of **multimorbidity as a dynamic and interactive framework**, in which conditions influence each other's progression and therapeutic response. Within this context, metabolic syndrome and chronic inflammation emerge as central drivers, while the microbiota and neuroregulatory systems act as modulators of intersystem communication. These mechanisms collectively shape the clinical presentation and trajectory of disease.

Importantly, the results support the superiority of **integrated, systems-based care approaches** over fragmented management strategies. By addressing shared underlying mechanisms rather than isolated symptoms, integrated care has the potential to improve diagnostic accuracy, enhance therapeutic coherence, and optimize patient outcomes. This approach does not replace specialization but rather redefines it within a coordinated and interconnected clinical model.

From an educational and clinical perspective, these findings underscore the need to strengthen systems-based thinking in internal medicine training. Teaching future physicians to recognize and interpret multisystem interactions is essential for improving clinical reasoning and patient-centered care. This is particularly relevant in healthcare settings where internal medicine plays a central role in coordinating complex cases.

In conclusion, the integration of gastrointestinal and urological perspectives within a systems-based framework provides a more comprehensive understanding of disease and represents a necessary evolution in internal medicine. Embracing this paradigm has the potential to transform both clinical practice and medical education, promoting a more holistic, efficient, and effective approach to patient care.

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