

Analysis of Undifferentiated Disease Consultation Patterns in General Internal Medicine Outpatient Clinics at County-Level General Hospitals: Post-Print

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Abstract

Background Medically Unexplained Diseases (MUD) are characterized by complex and diverse symptoms for which a clear diagnosis cannot be obtained or reasonably explained, along with frequent patient visits, imposing a substantial economic burden on individuals, families, and the healthcare system. **Objective** To investigate the current situation of MUD visits in the general internal medicine outpatient clinic of county-level general hospitals, provide epidemiological evidence, and propose a general practice diagnostic and therapeutic approach for MUD in county-level general hospitals, thereby providing a theoretical basis for standardized diagnosis and treatment of MUD. **Methods**

From January to March 2021, using a conditional sampling method, 45,439 patients with a total of 85,881 visits to the general internal medicine department of a Grade III, Class B general hospital in a county of Taizhou City, Zhejiang Province, from January 1, 2020 to December 31, 2020 were extracted from the Hospital Information System (HIS). The PRESUME screening method was used to screen adult MUD patients, collect patient data, and conduct analyses of population characteristics, distribution of visit times, and characteristic analysis of visit reasons. **Results** A total of 497 adult patients visited the general internal medicine outpatient clinic of the county-level general hospital for MUD, with an average of 2.23 visits per person and a mean age at presentation of (51.65 ± 15.89) years. Significant differences were observed in the age composition of the number of cases and visits among MUD patients of different genders in the general internal medicine outpatient clinic ($P < 0.01$). Comparisons of visit reasons among MUD patients of different genders showed that the number of visits due to anxiety state was higher in males than in females ($P < 0.05$). Comparisons of visit reasons among MUD patients of different ages revealed differences in age distribution for visits due to abdominal pain, anxiety state, and

cough ($P < 0.05$). Comparisons of gender and age among MUD visits in different quarters revealed no statistically significant differences; comparison of visit reasons across different quarters revealed differences in quarterly distribution for visits due to cough ($P < 0.05$). **Conclusion** Based on the survey findings on MUD visits in the general internal medicine outpatient clinic of county-level general hospitals, MUD is affected by multiple factors including gender, age, and season. Patients present frequently with diverse complaints, and the general internal medicine outpatient clinic cannot identify MUD patients at initial diagnosis and provide appropriate management. Therefore, further development of the general practice department is needed to provide more accurate diagnosis and treatment for MUD patients. The general practice department of county-level hospitals should become the primary-level diagnosis and treatment center for MUD, thereby comprehensively enhancing the social service effectiveness of county-level hospitals.

Full Text

Abstract

Background: Medically unspecified disease (MUD) is characterized by complex and diverse symptoms that cannot be clearly diagnosed or rationally explained, often leading to frequent hospital visits and imposing a heavy economic burden on individuals, families, and the healthcare system. **Objective:** To investigate the clinical presentation of MUD in general internal medicine clinics at county-level general hospitals, provide epidemiological data, and propose a general practice-based diagnostic and treatment framework for MUD in these settings, thereby establishing a theoretical foundation for standardized MUD management. **Methods:** From January to March 2021, we used conditional sampling to extract data from the Hospital Information System (HIS) for all 45,439 patients (85,881 total visits) who attended the general internal medicine clinic of a Grade B tertiary county general hospital in Taizhou, Zhejiang Province, between January 1 and December 31, 2020. Adult patients with MUD were identified using the PRESUME screening method, and their demographic characteristics, temporal distribution of visits, and reasons for consultation were analyzed. **Results:** A total of 497 adult patients visited for MUD, accounting for 1.09% of all general internal medicine patients, with 1,106 visits representing 1.29% of total clinic visits. The mean number of visits per patient was 2.23, and the mean age at presentation was (51.65 ± 15.89) years. Significant differences existed in age distribution and visit frequency between male and female MUD patients ($P < 0.01$). Among reasons for consultation, men had significantly more visits for anxiety than women ($P < 0.05$). Age-related differences were observed in visits for abdominal pain, anxiety, and cough ($P < 0.05$). No statistically significant differences were found in gender or age distribution across quarters; however, cough-related visits showed seasonal variation ($P < 0.05$). **Conclusion:** This survey demonstrates that MUD consultations at county general hospitals are influenced by multiple factors including gender, age, and season. Patients

present frequently with diverse complaints, and general internal medicine clinics struggle to identify and appropriately manage MUD at the first visit. Developing general practice departments to serve as primary MUD management centers in county hospitals is essential to provide accurate diagnosis and treatment, thereby enhancing the overall service capacity of these institutions.

Keywords: Medically unspecified disease; Medical treatment; County hospitals; Internal medicine clinic; General practice

Introduction

Medically unspecified disease (MUD) refers to conditions that cannot be medically explained, representing ultra-early or early-stage disease where physicians cannot establish a clear diagnosis or provide a rational explanation. Patients typically present with one or multiple symptoms, signs, or abnormal auxiliary test results and make repeated visits, yet physical examinations and investigations often yield normal or only mildly abnormal results that cannot be attributed to definite organic disease. MUD frequently coexists long-term with individuals and is commonly associated with psychological problems [?]. Clinically, MUD is extremely prevalent and can be classified into low-, moderate-, and high-risk categories based on symptom severity and duration [?]. Low-risk patients usually resolve spontaneously within two weeks, while moderate- and high-risk patients experience persistent symptoms that fail to self-resolve. Due to the lack of definitive diagnosis, their direct and indirect medical costs escalate through repeated investigations. A 1995 WHO study demonstrated that MUD is universally prevalent across different countries and cultures, imposing a substantial economic burden on patients, families, healthcare systems, and society [?]. An Indian survey reported a 24.6% prevalence of MUD in primary care settings [?], while Norwegian data indicated that 3% of MUD patients were moderate- to high-risk, with high visit frequency creating considerable pressure on physicians [?]. A 2018 analysis by the Department of General Practice at the First Affiliated Hospital of Zhejiang University School of Medicine found that 18.6%-21.3% of patients in general practice clinics presented with MUD [?]. Currently, MUD lacks unified diagnostic criteria, with most studies relying on self-developed statistics and no widely accepted screening tools, resulting in scarce and highly variable epidemiological data [?]. Recently, foreign researchers have proposed the PRESUME (preventive screening of medically unexplained physical symptoms) screening method based on the characteristic frequent presentation of MUD patients, which has been validated through five-year follow-up to effectively identify MUD, particularly moderate- and high-risk cases [?].

In a previous cross-sectional questionnaire survey of outpatients in general hospitals, Qian et al. [?] found that patients with somatic symptoms predominantly visited internal medicine departments. Although these patients often had coexisting psychological issues, most lacked mental health knowledge and initially

sought care in general internal medicine or other medical departments rather than psychiatric services. Therefore, this study selected patients from the general internal medicine clinic of a Grade B tertiary general hospital in Taizhou, Zhejiang Province in 2020, conducting a cross-sectional study using the PRESUME screening method to investigate the clinical presentation of MUD patients, provide epidemiological data for future research, and propose diagnostic and treatment recommendations for MUD in county general hospitals to establish a theoretical basis for standardized management.

1.1 Study Population

From January to March 2021, we used conditional sampling through the Hospital Information System (HIS) to include all patients who visited the general internal medicine clinic of a Grade B tertiary county general hospital in Taizhou, Zhejiang Province between January 1 and December 31, 2020. The total study population comprised 45,439 patients with 85,881 visits. Inclusion criteria were: (1) ≥5 visits to general internal medicine in 2020; (2) age ≥18 years; (3) no definitive disease diagnosis; and (4) presence of MUD symptoms (including fatigue, edema, weight loss, etc.) with the symptom as the reason for consultation. Exclusion criteria were: (1) patients with established diagnoses; and (2) patients with psychiatric conditions such as depression or schizophrenia requiring specialized care. This study was approved by the hospital ethics committee [Approval No.: 2021 Ethics Review Research No. (17)].

1.2 Research Methods

MUD patients were identified in the HIS using the PRESUME screening method, which demonstrates high specificity for moderate- and high-risk MUD patients but limited sensitivity for low-risk cases [?]. The selected subjects were re-evaluated by two general practitioners based on chief complaints, present illness history, and auxiliary examination data from medical records (with telephone follow-up for some patients). Patients who still could not receive a definitive diagnosis based on available information were confirmed as MUD cases for this study. Patient data were then collected for analysis of demographic characteristics, temporal distribution of visits, and reasons for consultation.

1.3 Data Collection

Using a double-entry method, two researchers collected and verified data through Excel software, extracting information on MUD patient gender, age, number of visits, consultation dates, and MUD symptoms (if multiple symptoms were present, the first-listed symptom was recorded) from the HIS system.

1.4 Statistical Analysis

Data were analyzed using SPSS 25.0 software. Measurement data were expressed as (mean \pm SD), and count data were described using frequency and composition ratio. Inter-group comparisons were performed using chi-square tests and rank-sum tests, with $P < 0.05$ considered statistically significant. For four-group comparisons, the test level was adjusted to 0.0083.

2.1 Age Composition by Gender Among MUD Patients

A total of 497 adult patients visited for MUD, representing 1.09% of all general internal medicine patients, with 1,106 visits accounting for 1.29% of total clinic visits. The average number of visits per MUD patient was 2.23, and the mean age at presentation was (51.65 \pm 15.89) years. The mean age was (55.25 \pm 17.29) years for female patients and (58.52 \pm 17.85) years for male patients ($\chi^2 = 21.769$, $P < 0.0001$), while men > 70 years had significantly more visits than women ($\chi^2 = 21.769$, $P < 0.0001$).

2.2 Comparison of Consultation Reasons by Gender and Age

Among general internal medicine MUD patients, 83 distinct reasons for consultation were identified. The top five most frequent reasons were: abdominal pain (126 visits, 11.39%), anxiety (93 visits, 8.41%), cough (69 visits, 6.06%), joint pain (64 visits, 5.79%), and constipation (61 visits, 5.52%). In gender-based comparisons, men had significantly more visits for anxiety than women ($P < 0.05$). Age-related differences were found in visits for abdominal pain, anxiety, and cough ($P < 0.05$). Specifically, abdominal pain visits were higher in the < 36 age group compared to 56-70 years ($\chi^2 = 9.030$, $P = 0.0027$) and > 70 years ($\chi^2 = 13.004$, $P = 0.0003$), and higher in the 36-55 age group compared to 56-70 years ($\chi^2 = 13.535$, $P = 0.0002$) and > 70 years ($\chi^2 = 18.161$, $P < 0.0001$). Anxiety-related visits were highest in the 56-70 age group compared to < 36 years ($\chi^2 = 9.819$, $P = 0.0017$) and 36-55 years ($\chi^2 = 15.7561$, $P = 0.0001$). Cough-related visits were more frequent in the > 70 age group compared to < 36 years ($\chi^2 = 15.250$, $P = 0.0001$), 36-55 years ($\chi^2 = 14.805$, $P = 0.0001$), and 56-70 years ($\chi^2 = 7.260$, $P = 0.0071$).

2.3 Seasonal Distribution of MUD Visits

No statistically significant differences were observed in gender or age distribution of MUD visits across quarters. However, seasonal variation was found in cough-related visits ($P < 0.05$). Post-hoc pairwise comparisons revealed that fourth-quarter visits were significantly higher than second-quarter ($\chi^2 = 7.565$, $P = 0.0060$) and third-quarter visits ($\chi^2 = 8.052$, $P = 0.0045$).

3.1 General Characteristics of MUD Patients

This survey found that the 36-55 age group had the highest number of MUD patients for both genders, consistent with international research showing higher MUD prevalence among middle-aged adults [?]. This may relate to patients' social and family roles, as individuals in this age range are primary breadwinners facing fast-paced lifestyles and intense competition, leading to central nervous system sensitization manifested as somatic symptoms. Additionally, population aging is increasingly prominent, with international studies reporting MUD prevalence of 1.5%-13.0% (median 5.4%) among older adults [?]. Pu and Zhang's research indicates that elderly patients with chronic diseases are more prone to anxiety and depression [?]. In this study, the >70 age group had significantly more male than female patients, possibly related to physiological and psychological changes in aging men, including alterations in physical appearance, strength, organ function, cognitive abilities, and quality of life. Matzkin et al. found that age-related changes in the hypothalamic-pituitary-testicular axis and declining testosterone levels may lead to sexual dysfunction, physical decline, diabetes, persistent late-life depression, cognitive impairment, sleep disorders, unexplained anemia of aging, osteoporosis, sarcopenia, and increased BMI, promoting the development of underlying chronic conditions and reducing overall health and quality of life in elderly men [?].

Regarding gender distribution, over half of MUD patients were male, which differs from previous epidemiological surveys and may relate to the continuous outflow of labor from the county, resulting in an increasing proportion of elderly male residents [?]. Gender distribution also varied across age groups, with women aged 36-55 showing higher MUD prevalence, though the difference was not statistically significant. Previous epidemiological studies have reported significantly higher MUD prevalence among women in this age group, with female patients presenting more symptoms and visiting more frequently, particularly non-specific general symptoms (94.6%) and various types of pain (93.7%) [?, ?]. Women in this age range often bear heavy social and psychological burdens as societal mainstays, experiencing greater emotional stress. Domestic research has found that women exhibit more somatic symptoms than men, such as fatigue, sleep problems, and dizziness, possibly because women are more likely to express negative emotions through somatic complaints due to different psychobiological processes [?].

3.2 Impact of Gender and Age on Reasons for MUD Consultation

MUD can involve multiple body systems, including digestive, psychological, respiratory, and musculoskeletal systems, with diverse and broad manifestations. In this survey of general internal medicine clinics, the primary reasons for consultation were abdominal pain, anxiety, cough, joint pain, and constipation. A 2019 Indian study of MUD prevalence in internal medicine clinics found that patients complained of an average of 13 ± 5 symptoms and visited repeatedly, with non-specific general symptoms and various types of pain being the main

complaints [?]. Yang et al. identified fatigue, sleep disturbance, weakness, indigestion, and dizziness as the top five symptoms among MUD patients in general hospitals [?]. Due to the diverse and unexplained nature of MUD symptoms, clinicians must possess not only extensive professional knowledge and skills but also a holistic diagnostic mindset.

Gender-based comparisons revealed that men had more anxiety-related visits than women, possibly because during the COVID-19 pandemic, socioeconomic impacts were substantial, and as primary family breadwinners, men experienced greater pressure and more severe anxiety. A Nigerian survey found that men experienced greater anxiety impacts than women during the pandemic, with low education, unemployment, unstable income, and older age being associated with more pronounced anxiety symptoms [?].

Age-related differences in consultation reasons showed that abdominal pain, anxiety, and cough varied across age groups. Abdominal pain was more common in the 36-55 age group than in adjacent age groups, likely because hormonal changes in this period trigger visceral pain, an important MUD mechanism. Research indicates that abdominal pain activates specific brain regions, causing intestinal hypersensitivity possibly related to sustained hyperexcitability of brainstem and thalamic nuclei and sensitization of the hypothalamus, amygdala, hippocampus, anterior insula, and anterior cingulate cortex—areas influenced by neuroendocrine, visceral sensory, and emotional-cognitive pain modulation [?, ?]. The 56-70 age group had the most anxiety-related visits, possibly due to declining physical function, increased health concerns, and reduced quality of life. A cross-sectional multicenter study found anxiety prevalence of 17.2% among adults aged 65-75 [?]. Cough symptoms were more prevalent in the <36 and 36-55 age groups compared to those >70, possibly because younger individuals have more active somatosensory cortices leading to enhanced somatosensory responses [?]. A domestic study found that most chronic cough patients were aged 30-40, with environmental and occupational exposures, smoking, and unhealthy lifestyles as contributing factors [?].

3.3 Seasonal Impact on MUD Presentation

No significant seasonal differences were found in gender or age distribution of MUD visits, which may relate to the multifactorial etiology of MUD, primarily involving physiological, psychosocial, and genetic factors [?]. However, international studies have found that when MUD coexists with psychological issues such as anxiety or low mood, seasonal differences become apparent, often with winter exacerbation [?]. This study found seasonal variation in cough symptoms, with significantly more visits in winter than autumn, likely related to dry, cold air irritating the respiratory tract. Previous epidemiological surveys have shown cough symptoms peak in winter and spring due to temperature fluctuations, increased allergens, and heightened airway sensitivity [?]. Clinicians should be aware of MUD's seasonal characteristics, promptly exclude critical conditions, and implement early assessment, identification, communication, and continuous

management.

An Italian 9-year observational and retrospective study on MUD noted that most cases do not present with single somatization symptoms; rather, physiology, personality traits, life experiences, health perceptions, and interactions with healthcare providers all play important roles in MUD development [?]. These patients account for 25-50% of visits to general practice departments. Huang and He found that MUD patients receive more optimized solutions and higher satisfaction when managed in general practice departments, which maintain close connections with multiple disciplines and can integrate hospital resources to provide multidisciplinary, comprehensive care [?]. A study on MUD management strategies proposed that general practitioners occupy a central role in MUD diagnosis and treatment, yet systematic, standardized management protocols remain underdeveloped [?]. Developing management procedures and training programs is crucial to help general practitioners understand MUD characteristics and establish specialized MUD clinics, which would improve patient belongingness, compliance, reduce pressure on general outpatient clinics, and explore suitable development directions for MUD management in county general hospitals. Public awareness campaigns through social and media channels could increase understanding of MUD and the value of general practice in its management, guiding patients to appropriate care settings, simplifying processes, and maximizing patient benefits.

Conclusion

Currently, MUD patients make repeated visits to county hospitals, creating substantial pressure on the healthcare system that general internal medicine clinics cannot adequately address. MUD presentations are frequent and diverse, influenced by gender, age, season, and other factors, without established standardized management protocols. Future development of general practice departments in county hospitals should establish comprehensive MUD management frameworks to provide multidimensional, integrated, and efficient care. Due to MUD' s complex symptomatology, patients may seek care in various specialties; thus, screening only general internal medicine patients has sampling limitations and cannot represent the entire hospital or county MUD population. Future research should sample multiple hospitals across the county to expand sample size and improve representativeness. This study only analyzed single symptoms without integrating or categorizing symptom clusters; future studies should examine whether specific symptom patterns differ across demographic characteristics and consultation periods. Additionally, this study' s assessment criteria were relatively subjective; more objective diagnostic criteria and higher-sensitivity screening tools should be developed.

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Author Contributions

Lou Zheng, Liu Ying, and Ren Jingjing were responsible for conceptualization and design. Lou Zheng conducted investigation, data collection and curation, statistical analysis, interpretation of results, and manuscript drafting. Lou Zheng, Liu Ying, and Ren Jingjing contributed to language polishing, translation revision, data analysis conceptualization, and manuscript revision. Ren Jingjing provided overall supervision and project administration.

Conflict of Interest

The authors declare no conflicts of interest.

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