

Table 2. Regression models, testing for associations between the nine domains of the HLQ and clinical and non-clinical outcomes, adjusted for age and gender.

	1. HPS	2. HSI	3. AMH	4. SS	5. CA	6. AE	7. NHS	8. FHI	9. UHI
Severity of self-reported disease activity in last 2 weeks (β)	-7.85 (-10.90 - -4.80)	-17.11 (-20.58 - -13.65)	-8.63 (-13.05 - -4.22)	-12.03 (-15.41 - -8.64)	-4.43 (-8.47 - -0.39)	-9.93 (-12.17 - -7.69)	-11.29 (-13.75 - -8.83)	-12.83 (-15.79 - -9.86)	-12.58 (-15.75 - -9.41)
Tender joint count in last 2 weeks (β)	-1.67 (-2.46 - -0.88)	-3.17 (-4.10 - -2.25)	-1.22 (-2.38 - -0.05)	-2.18 (-3.07 - -1.29)	-0.25 (-1.31 - 0.80)	-2.21 (-2.79 - -1.62)	-2.35 (-2.99 - -1.70)	-2.70 (-3.47 - -1.92)	-3.05 (-3.87 - -2.22)
Swollen joint count in last 2 weeks (β)	-1.30 (-2.00 - -0.60)	-2.04 (-2.86 - -1.23)	-1.39 (-2.43 - -0.34)	-1.74 (-2.54 - -0.94)	-0.64 (-1.58 - 0.30)	-1.53 (-2.06 - -1.00)	-1.76 (-2.36 - -1.20)	-1.93 (-2.61 - -1.25)	-1.96 (-2.70 - -1.23)
Corticosteroid use in last 2 weeks (OR)	1.47 (1.03 - 2.09)	0.80 (0.53 - 1.19)	0.88 (0.54 - 1.45)	1.02 (0.69 - 1.50)	0.78 (0.50 - 1.22)	0.91 (0.70 - 1.17)	0.86 (0.65 - 1.14)	0.55 (0.40 - 0.76)	0.62 (0.44 - 0.88)
Current csDMARD use (OR)	1.31 (0.95 - 1.80)	1.34 (0.92 - 1.94)	1.08 (0.68 - 1.71)	1.48 (1.03 - 2.13)	0.87 (0.57 - 1.32)	1.30 (1.03 - 1.65)	1.28 (0.99 - 1.67)	1.09 (0.79 - 1.49)	1.14 (0.82 - 1.60)
Current b/tsDMARD use (OR)	1.70 (1.28 - 2.25)	1.23 (0.90 - 1.69)	1.12 (0.77 - 1.64)	1.00 (0.74 - 1.34)	1.20 (0.84 - 1.72)	1.12 (0.91 - 1.37)	1.10 (0.88 - 1.38)	0.99 (0.76 - 1.30)	1.02 (0.77 - 1.36)
RDCI (0-5) (β)	-0.01 (-0.10 - 0.08)	-0.01 (-0.11 - 0.10)	-0.05 (-0.18 - 0.08)	0.09 (-0.01 - 0.19)	0.06 (-0.06 - 0.18)	-0.06 (-0.13 - 0.01)	-0.06 (-0.14 - 0.01)	-0.09 (-0.18 - 0.00)	-0.15 (-0.25 - -0.05)
Employment status (OR)	1.06 (0.81 - 1.36)	1.09 (0.80 - 1.50)	0.72 (0.49 - 1.07)	0.57 (0.37 - 0.88)	0.96 (0.67 - 1.37)	1.11 (0.91 - 1.36)	1.23 (0.98 - 1.54)	1.44 (1.10 - 1.88)	1.38 (1.04 - 1.84)
Absenteeism (OR)	0.72 (0.48 - 1.07)	0.35 (0.21 - 0.57)	0.72 (0.41 - 1.26)	0.39 (0.24 - 0.63)	0.77 (0.46 - 1.31)	0.65 (0.49 - 0.87)	0.62 (0.45 - 0.84)	0.51 (0.35 - 0.74)	0.53 (0.35 - 0.80)
Presenteeism (OR)	0.61 (0.45 - 0.84)	0.21 (0.14 - 0.31)	0.58 (0.37 - 0.88)	0.39 (0.28 - 0.56)	0.80 (0.54 - 1.19)	0.51 (0.41 - 0.64)	0.45 (0.35 - 0.57)	0.35 (0.26 - 0.48)	0.43 (0.31 - 0.60)
Work Productivity Loss (β)	-0.36 (-0.57 - -0.14)	-1.07 (-1.34 - -0.81)	-0.33 (-0.64 - -0.01)	-0.63 (-0.88 - -0.39)	-0.21 (-0.50 - 0.08)	-0.45 (-0.81 - -0.30)	-0.53 (-0.69 - -0.37)	-0.72 (-0.92 - -0.52)	-0.60 (-0.85 - -0.36)
Activity Impairment (β)	-0.32 (-0.44 - -0.19)	-0.77 (-0.91 - -0.62)	-0.42 (-0.60 - -0.23)	-0.48 (-0.62 - -0.33)	-0.17 (-0.33 - 0.00)	-0.44 (-0.55 - -0.34)	-0.52 (-0.63 - -0.40)	-0.60 (-0.72 - -0.47)	-0.58 (-0.72 - -0.44)
PHQ-2 (β)	-0.44 (-0.61 - -0.27)	-0.93 (-1.13 - -0.74)	-0.82 (-1.08 - -0.57)	-0.89 (-1.08 - -0.71)	-0.34 (-0.56 - -0.11)	-0.55 (-0.88 - -0.43)	-0.66 (-0.79 - -0.52)	-0.75 (-0.91 - -0.58)	-0.78 (-0.95 - -0.60)
GAD-2 (β)	-0.43 (-0.61 - -0.26)	-0.87 (-1.07 - -0.66)	-0.60 (-0.85 - -0.34)	-0.73 (-0.93 - -0.54)	-0.20 (-0.44 - 0.03)	-0.53 (-0.67 - -0.40)	-0.66 (-0.81 - -0.52)	-0.83 (-1.00 - -0.66)	-0.87 (-1.06 - -0.69)

Outcomes of logistic regression models are presented as odds ratios (OR) and 95% confidence intervals (CI); outcomes of linear regression models are presented as beta coefficients (β) and 95% CI. csDMARD: conventional synthetic disease-modifying anti-rheumatic drug. b/tsDMARD: biologic or targeted synthetic disease-modifying anti-rheumatic drug. RDCI: Rheumatic Diseases Comorbidity Index. PHQ-2: 2-item Patient Health Questionnaire. GAD-2: 2-question Generalised Anxiety Disorder 2-item questionnaire.

Histological assessment of inflammatory infiltrates in interstitial cystitis/bladder pain syndrome (IC/BPS): a comparative study of mast cell quantification techniques
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Introduction
Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic disease of unknown aetiology that affects the normal pathophysiology of urinary bladder.¹ Given the complex nature of pathogenesis, there are no universally accepted clinical or histological diagnostic criteria for IC/BPS. The central role of urothelial inflammation and mast cell activation in the detrusor muscle have been histologically confirmed in IC/BPS cases.^{2,3} However, there is no standardised diagnostic technique for evaluating, interpreting and reporting histopathological findings, such as inflammatory markers, in IC/BPS. Therefore, this retrospective study aimed to assess inflammatory cell infiltrate to better understand the role of inflammation to provide diagnostic value in histopathology reports for improved patient treatment and to compare histochemical and immunohistochemical stains for efficiency and sensitivity in detection and quantification of mast cells in detrusor muscle.

Methods
This retrospective study analysed 26 formalin-fixed paraffin-embedded bladder biopsies/tissues with confirmed IC/BPS. Inflammation was graded as acute, chronic or mix based on present inflammatory cells using Haematoxylin and Eosin staining. Eosinophils were recorded as present or absent. Mast cells were detected using three techniques: Toluidine Blue, Artisan Giemsa, and anti-CD117 immunohistochemistry. A four-point grading system (0: <5, 1: 6–10, 2: 11–20, 3: >20 mast cells/high-power field) was applied. Sensitivity was calculated based on positive mast cell detection. Lymphocyte subsets were assessed using anti-CD3 (T lymphocytes) and anti-CD20 (B lymphocytes) antibodies, and predominance was recorded in cases with moderate-to-severe inflammation.

Results
Chronic inflammation was observed in 96.2% of cases, with eosinophilic infiltration present in 76.9% (Fig 1). CD117 immunohistochemistry demonstrated the highest sensitivity for mast cell detection (73.1%) compared with Toluidine Blue (50%) and Artisan Giemsa (26.9%) (p=0.002) (Fig 2). Definite mast cell infiltration was found in 46.2% of cases, all of which were eosinophil-positive. Among these, 83.3% showed T lymphocyte predominance within the detrusor muscle. These results suggest that eosinophils and T-lymphocytes may have a synergistic role in chronic bladder inflammation.

Conclusion
This study confirmed the importance of inflammatory cell infiltrates, particularly lymphoplasmacytic, eosinophilic and mast cell components, in the histological evaluation of IC/BPS, consistent with published studies.^{1–5} Anti-CD117 staining was the most sensitive and reproducible method for detecting mast cells, supporting its inclusion in routine histopathological assessment. The observed T lymphocyte predominance in mast cell-positive, eosinophil-rich cases suggests a potential immunological pattern that may inform future diagnostic and therapeutic strategies. Standardising the evaluation of inflammatory infiltrates and including mast cell and lymphocyte profiling in pathology reports could enhance diagnostic precision and guide patient management in IC/BPS.

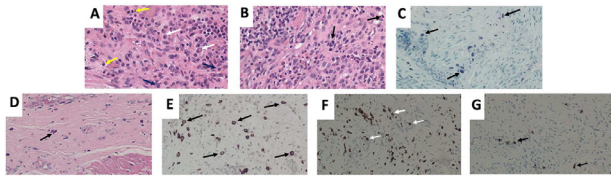


Fig 1. (A) Mix inflammatory infiltration (neutrophils, yellow; lymphocytes, dark blue; plasma cells, white arrows). (B) Eosinophilic infiltration (black arrows). Mast cells in (C) Toluidine Blue (black arrows), (D) Giemsa (Artisan) (black arrows) and (E) anti-CD117 antibody staining (black arrows). (F) T lymphocytes (white arrows). (G) B lymphocytes (black arrows).

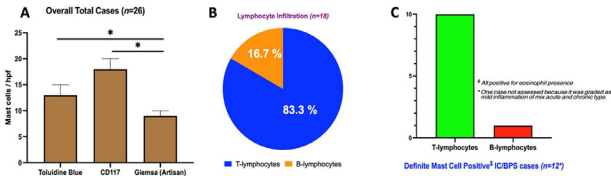


Fig 2. (A) Quantitative comparison of mast cell detection using three staining techniques: Toluidine Blue, Artisan Giemsa, and anti-CD117 immunohistochemistry, in IC/BPS cases (n=26). (B) Analysis of lymphocyte subset predominance (T vs B lymphocytes) in IC/BPS cases exhibiting moderate-to-severe inflammation. (C) Subset analysis of lymphocytic profiles in IC/BPS cases with confirmed mast cell positivity (n=12).

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How serious are ‘serious non-specific symptoms (SNSS)’? Evaluation of the introduction of a local SNSS pathway, and the pick-up rate of cancers, within this population
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Introduction

As part of the NHS Long-Term Plan, ambitions were set that, from 2028, an extra 55,000 people will survive for 5 years or more following cancer diagnosis, through earlier detection. ‘Serious non-specific symptom’ (SNSS) pathways were developed to aid GPs in referring patients

with more vague symptoms, concerning for malignancy, that may not already fit into a system specific cancer referral pathway.¹

Within our Trust, GPs can refer for an urgent computed tomography (CT) chest, abdomen and pelvis, with results reviewed in a weekly multi-disciplinary team (MDT) meeting. Following this, patients are either discharged back to their GP with advice, or referred on to appropriate cancer pathways. Benign disease is also highlighted to GPs, to consider referral to the appropriate specialty if clinically indicated.

This audit aimed to look at those patients referred to our local SNSS pathway and evaluate cancer pick up rate, type of cancers and prevalence of benign disease. To date, there are few published data on this within the UK, although one Danish study detected a cancer pick-up rate of 11–20%.²

Materials and Methods

We designed a retrospective audit looking at all patients referred via the SNSS pathway from February 2023 to September 2023 in South Tyneside and Sunderland NHS Foundation Trust. Electronic notes were then reviewed, and we looked at referral indications, inappropriate referrals (those meeting pre-existing suspected cancer pathways), cancer pick-up rate, cancer type and incidence of metastatic disease.

Results and Discussion

502 patients were reviewed, over 30 MDT meetings. This was evenly split between male (45%) and female (55%) patients, with an average age of 71 years. The most common symptom prompting referral was weight loss, in 74.1% of referrals. Of these patients, 7.5% were diagnosed with cancer. Other common symptoms included fatigue (22.5%), abdominal pain (20.7%), anorexia (13.9%) and generalised pain (13.1%). The overall cancer pick-up rate was 8.6%, with 43 patients found to have a cancer diagnosis.

Almost 6% of all patients were inappropriately referred to this pathway, having met criteria for pre-existing cancer pathways. However, even excluding these patients, the overall pick-up rate remained at 8.4%.

The most common primary cancers were upper gastrointestinal (25.6%), lung (23.3%) and haematology (11.6%). 37.2% of all patients with cancer had metastatic disease. Benign pathology was detected in 65% of patients.

Conclusion

Overall cancer-pick up rates in our audit suggest that the SNSS pathway has a similar pick-up rate to existing urgent suspected cancer pathways in the NHS (around 7%). This shows that the pathway is valuable in picking up patients with vague symptoms who may not qualify for existing pathways but still have a high incidence of cancer. This provides a valuable tool for GPs to use when they have clinical concern about cancer within non-specific presentations. There are areas for improvement, with 5.6% of inappropriate referrals, potentially highlighting a lack of awareness of pre-existing cancer pathways. We suggest that further national analysis could be done on long-term patient outcomes, and effectiveness of SNSS pathways, including 5-year survival, in such a novel pathway.

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