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Inflammatory proteins in the urine and bladder tissue of women with lower urinary tract symptoms

Submission date
24/11/2024

Recruitment status
No longer recruiting

Registration date
28/11/2024

Overall study status
Completed

Last Edited
28/11/2024

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Lower urinary tract symptoms (LUTS), such as urinary urgency, urge incontinence, chronic bladder related, and recurrent urinary tract infections affect more than half of the female population worldwide. Despite their prevalence, the underlying mechanisms that cause LUTS are poorly understood, which is likely a reflection of a multifactorial aetiology. Many women will additionally experience overlapping symptoms and conditions of the bladder in their lifetime.

Various bladder conditions have been found to be linked to a pro-inflammatory state within the bladder itself. Cell signalling proteins called cytokines have been found to be elevated in the urine and in bladder tissue samples of those with LUTS compared to those without. However, how various cytokines may be related to particular LUTS remains unclear. We hypothesise that different inflammatory pathways may be responsible for causing LUTS in women with overactive bladder syndrome (OAB) and bladder pain syndrome (BPS). We also hypothesise that women with acute urinary tract infection with or without a diagnosis of OAB or BPS may leave a further additional differing cytokine profile signifying an infective process.

The purpose of this study is to build on existing research that has been carried out in the field of biomarkers, urinary cytokines, and bladder pain syndrome. In our study we aim to look not only at women with chronic bladder pain but with other chronic lower urinary tract symptoms to understand whether there is an inflammatory component and then try and better understand the pathophysiology and pathogenesis of these conditions- especially in bladder pain syndrome for which the underlying pathophysiology remains unknown. Bladder conditions in women are not only well understood but often symptoms can overlap over time. Currently treatment is often offered in a "trial" -where a treatment is tried and if it does not help then another is tried. Better than this method would be the ability to target treatment. With better understanding of the inflammatory pathways that underpin chronic lower urinary tract symptoms this could be achieved in the future. This study aims to further our understanding of these bladder symptoms and conditions.

Who can participate?
Any women with lower urinary tract symptoms that have been ongoing for 3months or more who has been referred to St Mary's Hospital London for the investigation and management of these symptoms. Participants will already have decided that they are willing to have their lower urinary tract symptoms investigated with a procedure called a cystoscopy, where the inside of the bladder is looked at via a camera and then small bladder tissue samples are taken. All participants for this study are undergoing rigid cystoscopy with bladder biopsies under a general anaesthetic.

What does the study involve?
The study involves participants filling out three validated questionnaires about their bladder symptoms: 1) the King's Health Questionnaire, 2) the O'Leary/Sant interstitial cystitis index, 3) the International Consultation of Incontinence Questionnaire-female lower urinary tract symptoms- ICIQ-fluts. Participants then undergo rigid cystoscopy and bladder biopsy- at the time of cystoscopy a sterile sample of urine is collected and an extra tissue

What are the possible benefits and risks of participating?
Participants are all already undergoing cystoscopy procedures with bladder biopsies already being taken- however extra tissue samples are taken for research which increases the risk of bleeding from the bladder and the risk of bladder perforation. These risks are very low less than 1/1000.
There are no short-term benefits to participation. Long-term benefits could include the availability of more targeted treatment for urinary symptoms based on the inflammatory profile found.

Where is the study run from?
St Mary's Hospital, Imperial College Healthcare Trust, London (UK)

When is the study starting and how long is it expected to run for?
April 2023 to January 2026

Who is funding the study?
The Charm Charity and BSUG-the British Society of Urogynaecology (UK)

Who is the main contact?
Dr Bernadette Lemmon, blemmon@nhs.net

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
351850

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
URO_VK_16_041-Uro-gynaecology collection

Study information

Scientific Title
Urinary and bladder cytokine expression in women with lower urinary tract symptoms

Acronym
CytoLUTS

Study objectives
1. Women with lower urinary tract symptom have raised inflammatory cytokines when compared with healthy controls.
2. Women with bladder pain syndrome, overactive bladder syndrome, and those with recurrent urinary tract infections display different and distinct patterns of inflammatory cytokine expression.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 16/11/2016, Imperial College Healthcare Tissue Bank (Department of Surgery and Cancer, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF, United Kingdom; +44 7711701382; geraldin.thomas@imperial.ac.uk), ref: URO_VK_16_041- Uro-gynaecology collection

2. notYetSubmitted 23/11/2024, Health Research Authority and Health and Care Research Wales (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom)

Study design
Single centre observational cross-sectional cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Identifying and understanding inflammatory changes in the urine and bladder tissue of women with chronic lower urinary tract symptoms

Interventions
Women recruited for this study will be asked to fill out three validated symptom questionnaires about their chronic lower urinary tract symptoms: 1) The O'Leary Sant Interstitial Cystitis Index (ICSI) 2) the King's Health Questionnaire (KHQ) 3) The international Consultation on Incontinence Questionnaire-female lower urinary tract symptom modules (ICIQ-fluts).

All women recruited will already be undergoing cystoscopy and bladder biopsies for investigation of their bladder symptoms. At the time of cystoscopy a sterile sample of urine is taken and two extra bladder biopsies. Multiplex sandwich ELISA assaying techniques are used for the detection of a panel of inflammatory cytokines in the paired urine and bladder tissue samples and compared with healthy controls without chronic urinary tract symptoms.

Intervention Type
Other

Primary outcome(s)
Inflammatory cytokine expression in urine and bladder tissue measured at the time of cystoscopy using a sterile sample of urine and two extra bladder biopsies. Multiplex sandwich ELISA assaying techniques are used for the detection of a panel of inflammatory cytokines in the paired urine and bladder tissue samples and compared with healthy controls without chronic urinary tract symptoms.

Key secondary outcome(s))
Chronic lower urinary tract symptoms measured at baseline
1. The O'Leary Sant Interstitial Cystitis Index (ICSI)
2. The King's Health Questionnaire (KHQ)

3. The international Consultation on Incontinence Questionnaire-female lower urinary tract symptom modules (ICIQ-fluts)

Completion date
31/01/2026

Eligibility

Key inclusion criteria
1. Women with significantly bothersome lower urinary tract symptoms lasting for over 3 months
2. Women who are already undergoing cystoscopy and bladder biopsy under a general anaesthetic for the investigation of lower urinary tract symptoms
3. Women aged 18 or older
4. Women with the capacity to consent to take part in research themselves
5. Women able to complete validated symptom questionnaires in English
6. Women who have signed a valid written consent form for the provision of extra samples for research under the Imperial College Healthcare Tissue Bank Ethics

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
100 years

Sex
Female

Key exclusion criteria
1. Women under the age of 18 years
2. Women who are unable to complete validated questionnaires in English
3. Women without capacity to consent themselves for research
4. Women who have undergone previous continence procedures
5. Women with a history of urological malignancy
6. Women undergoing current treatment for urological malignancy

Date of first enrolment
01/08/2023

Date of final enrolment
30/01/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital, Imperial College Healthcare NHS Trust
Praed Street
London
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research organisation

Funder Name
British Society of Urogynaecology

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be initially available upon request from Dr Bernadette Lemmon, email: blemmon@nhs.net. At the end of the study datasets generated will be sorted in a non-publicly available repository - the Imperial College Tissue Bank.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1	27/11/2024	28/11/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1	27/11/2024	28/11/2024	No	No