

Incidence Of Lactobacilli Infection In Uti Among Diabetic Women

M.V shreejha ¹, Dr. Muralidharan N.P ^{2*}, Dr. Geetha.R.V ³

¹ Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences(SIMATS), Saveetha University, Chennai, Tamilnadu, India.

^{2*} Associate Professor, Department of Microbiology, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Chennai, TamilNadu, India.

³ Professor, Department of Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences(SIMATS), Saveetha University, Chennai, Tamilnadu, India.

E-mail: ¹ 151901062.sdc@saveetha.com , ^{2*} muralidharan@saveetha.com , ³ geetha@saveetha.com

Abstract

AIM

The aim of the study is to find out the incidence of UTI with lactobacilli in diabetic women.

MATERIALS AND METHODS

The study is done in patients visiting the general OP department. Samples were collected from patients who are clinically proven diabetic. Morning mid stream urine samples were collected, PH is noted first. Samples were then inoculated on nutrient agar and macconkey agar and incubated at 37 deg.C for 24 hours. The growth on macconkey agar was identified by gram staining for the presence of long filamentous gram positive bacilli. The results were tabled and analysed.

RESULTS

Among the total number of 204 patients reported with the symptoms of urinary tract infections, 14 of them were positive for Lactobacillus infection (6.9 %), including 2 male and 12 female.

DISCUSSION

In this study it is found that lactobacilli is significantly contributing to the pathogenesis of UTI in diabetic patients. Due to the metabolic changes and decrease in the pH of urine, acidophilic bacteria can easily grow in urine.

CONCLUSION

Acidic pH in urine predisposes to the growth of Lactobacilli in urine in diabetic patients. So keeping blood sugar under control will prevent colonization of lactobacillus sp in the urinary tract.

Keywords: Lactobacilli, diabetic women, Innovative study

Introduction

Urinary tract infection (UTI) in women is the most common auto infectious disease. The type of urinary tract infections are urethritis – infection occurs at the urethra, cystitis – infection occurs at bladder, pyelonephritis – infection occurs at kidneys, vaginitis – infection occurs at vagina. There are two types of infection in UTI ascending and descending types of infections, the steps for ascending infections, the bacteria will first affect urethral mucosal epithelial cells and then travel to the bladder and cause bacterial infections. Descending infections are the hematogenous spread of bacteria from the primary source which is located somewhere

else in the body. (Medina and Castillo-Pino, 2019) In normal healthy women, the vulvar area anterior to the vagina sustains a group of bacterial species, lactobacilli being dominant members. In vitro studies results said that the lactobacilli may inhibit the growth of *Escherichia coli* for several reasons: a) nutritional factors competition, b) production of simple bacteriostatic compounds (e.g. lactic acid), c) competitive coaggregation to other bacteria and to uroepithelial cells, and d) production of specific growth inhibitors for other bacteria. In a previous study it has been said that uncomplicated lower UTI remains one of the most common infections in primary care. UTI is a common source of infection in children and infants and the bacterial infection occurs at age < 2 years for the children. During the first six months of the infant's life, UTIs are more common in boys. (Chee Wei Tan, 2016). However the reason for this complication is still uncertain. UTIs are rare in males less than 50 years but increase in the case of prostatitis, epididymitis, orchitis, cystitis, urethritis, and urinary catheters. UTIs in males can be complicated when they are associated with anatomic abnormalities, requiring surgical intervention to prevent sequelae (Gelotar *et al.*, 2012). According to the female, they are more prone to the UTI infection, considering the female urethra due to the hormonal activity and most common during pregnancy. Most common cause of UTIs are gastrointestinal bacteria, which infect the urethra through contaminating the area that surrounds the rectum and spreading to the bladder. In addition, the factors increase the rate of infection of the urinary tract including sexual factors, urine factors, osmolality of urine, introital factors, vaginal pH, and secretor state. Some of the main and most common causes of UTIs are "*Escherichia coli*, *Staphylococcus spp.*, *Streptococcus spp.*, *Proteus spp.*, *Klebsiella spp.*, *Corynebacterium*, *Neisseria* and *Pseudomonas spp.*". (Almukhtar, 2018). In old age people's asymptomatic bacteriuria is transient as it resolves without any treatment plan. (Mody and Juthani-Mehta, 2014) UTI is more common in diabetics because the patients with diabetes are more prone to get urinary tract infection due to frequent urination and high blood sugar level. The high sugar level gives a favorable growth environment to the pathogens. Early diagnosis and proper medication are necessary for management of urinary tract infection in diabetic patients. Are diabetics more prone to candida because of higher levels of glucose in the blood make candida all the more likely, so diabetics who have difficulty controlling their blood sugar may find themselves particularly prone to yeast infections. Diabetes can also lead to kidney complications or increase risk of infections of the urinary tract, both of which can make urine appear cloudy. Urinary tract infections are common complications of diabetes. That's because high blood sugar can lead to sugar in your urine, and sugar is a breeding ground for bacteria. If your bladder doesn't empty completely when you urinate, bacteria can hang around in your urinary tract even longer.

The influence of glucose metabolism is seen in many infectious diseases, making diabetic patients more vulnerable to sepsis and other serious sequelae of bacterial invasion. Vaginal candidiasis is a common problem if the glycemia is poorly controlled. The level of glucose concentration in the blood after ingestion of sugar seems to explain an increased likelihood of recurrent infection. Specific immune aberrations, such as an elevated T-helper 2 response and a blunted T-helper 1 response, leading to tolerance, may result in chronic recurrent vulvovaginal candidiasis. In such patients, a low-grade infection with frequent exacerbations bladder colonization. Lethal emphysematous nephritis due to *Candida albicans* organ-forming bacteria such as *Escherichia coli*, *Klebsiella*, *Proteus*, streptococci, or enterococci are known to occur in diabetic patients. UTIs in diabetic patients are difficult to destroy and need longer and intense antibiotic therapy. Awareness of the increased UTIs, in frequent screening, and prolonged treatment in case of cystitis. To prevent UTI and bacterial vaginal infections estrogen therapy is very much as important in antibiotic therapy. Catheterization is limited since it promotes infection more in diabetic patients than in nondiabetic patients.

Diabetes mellitus (DM) is one of the most challenging health problems of the current generation. It affects every aspect of people's lives, including quality of life, employment and also causes premature death. DM is

considered as the 5th leading cause of death in the developing countries. DM patients are more prone to have various kinds of infections than non-diabetics. This high infection in diabetes mellitus affects the immune functions like polymorphonuclear leukocyte function, adhesion phagocytosis, chemotaxis and impaired antioxidant system. (Nitzan *et al.*, 2015) All these changes in the patient's body make the diabetic patients prone to infections such as UTI, RTI, skin and soft tissue infections. The prevalence of UTI infection is high in DM patients. DM is considered as a major risk factor for UTIs. Patients with diabetic mellitus are more prone to get UTI infection than non-diabetic.

UTIs are higher among diabetics than non-diabetics. (Hoepelman, no date) Patients with type 2 diabetes mellitus are more prone to infections. Various reasons include poor immune system, poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy. All these pathogenesis plays a major role in urinary tract infections (UTI) in diabetic patients. Factors that were found to be in the risk for UTI in diabetics include age, metabolic control, and long term complications. (Geerlings, 2008) The Serious complications in UTI are emphysematous cystitis and pyelonephritis, renal abscesses and renal papillary necrosis, are mostly seen in type 2 diabetes than in the general population. Type 2 diabetes is also a risk factor for fungal UTI infection. mostly caused by *Candida*. Diabetes is also associated with worse outcomes of UTI, including longer hospitalizations and increased mortality. UTIs are caused by both Gram-negative and Gram-positive bacteria, as well as some specific type of fungi. The most common causative agent for both uncomplicated and complicated UTIs is uropathogenic *Escherichia coli* (UPEC). For the agents involved in uncomplicated UTIs, UPEC is followed in prevalence by *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, group B *Streptococcus* (GBS), *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida* spp. For complicated UTIs, the order of prevalence for causative agents, following UPEC as most common, is *Enterococcus* spp., *K. pneumoniae*, *Candida* spp.,

S.aureus, *P. mirabilis*, *P. aeruginosa* and GBS. The aim of our study is Incidence of lactobacilli in UTI among diabetic females. (Saliba *et al.*, 2015) (Flores-Mireles *et al.*, 2015) Our team has extensive knowledge and research experience that has translate into high quality publications (Priyadharsini *et al.*, 2018; Vijayashree Priyadharsini, Smiline Girija and Paramasivam, 2018; Ramalingam, Selvi and Jayaseelan, 2019; Vijayashree Priyadharsini, 2019; Girija, Shankar and Larsson, 2020; Jayaseelan and Arumugam, 2020; Kumar, Girija and Priyadharsini, 2020; Mathivadani, Smiline and Priyadharsini, 2020; Paramasivam and Vijayashree Priyadharsini, 2020; Paramasivam, Priyadharsini and Raghunandhakumar, 2020; Paramasivam, Vijayashree Priyadharsini and Raghunandhakumar, 2020; Ushanthika *et al.*, 2021), (Reddy *et al.*, 2020; Teja and Ramesh, 2020; Barma *et al.*, 2021; Samuel, 2021; Samuel *et al.*, 2021). (Jayaseelan and Paramasivam, 2020) (Iswarya Jaisankar *et al.*, 2020) (Girija, 2021)

MATERIALS AND METHODS

This study is done in patients visiting the general OP department. Samples were collected from patients who are clinically proven diabetic. The patients were informed about the study and after obtaining the informed consent, early morning mid stream urine samples were collected in sterile disposable plastic containers and transported to the microbiology department. Samples were stored at 4 deg.C till it was processed. Samples were inoculated on Nutrient agar, MacConkey agar, Blood agar and incubated at 37 deg.C for 48 hours. The method used for enumeration is the calibrated loop method. A loop with 4 mm diameter is used to inoculate the samples. The organisms grown were identified based on the standard microbiological protocol. The details of the organisms grown and the colony count were tabulated for analysis. All the organisms grown were identified with the standard microbiological protocol. The growth on MacConkey agar was identified by gram's staining for the presence of long filamentous gram positive bacilli. The colonies are biochemically confirmed as Lactobacilli. The results were tabulated and analysed.

All urine samples were checked with narrow range pH paper. Then 4 - 5 ml of urine is transferred to a test tube and centrifuged at 1500 rpm for 3 mins and the supernatant discarded and the sediments were examined under 45X objective of the microscope. All samples were screened for the presence of long filamentous gram positive bacteria and other organised structures in the deposits.

RESULTS

This study is conducted in patients attending the OP clinic attached to the hospital. In this 204 patients were included. Patients were selected randomly. The inclusion criteria is, they should have been declared as diabetic. No antibiotics taken for the past 48 hrs. Among the samples

collected 14 patients were positive for lactobacillus culture. Their urine samples have shown plenty of pus cells. The pH testing of the samples have shown that their pH is all acidic and ranges from 5.0 - 7.0.

No. patient samples collected	Lactobacillus infection	Percentage Association
204	14	6.9

Table 1: Table shows no. of patients samples collected and lactobacillus association

SL.NO	TOTAL CFU	PH RANGE
1	100000	5.6
2	1000	6.5
3	100000	5.2
4	1000	7.0
5	1000	6.2
6	1000	5.8
7	100000	5.5
8	100000	5.6
9	1000	6.5
10	100000	5.8
11	100000	5.0
12	100000	5.2
13	100000	5.5
14	100000	5.2

Table 2 : Represent pH Association with lactobacillus count

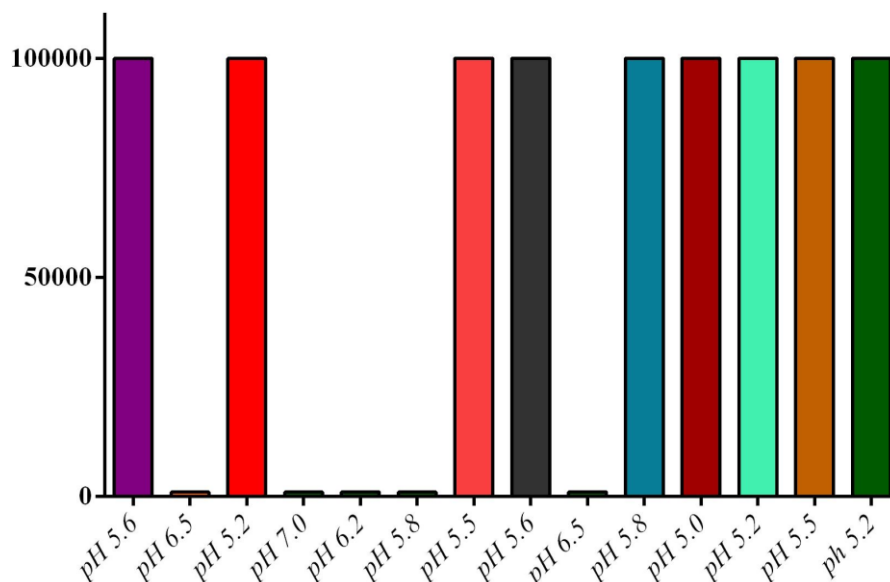


Figure 1: Bar diagram showing the total CFU with corresponding pH. X axis shows pH range and the Y axis represents the total CFU.

- Males associated with lactobacillus infection
- Females associated with lactobacillus infection

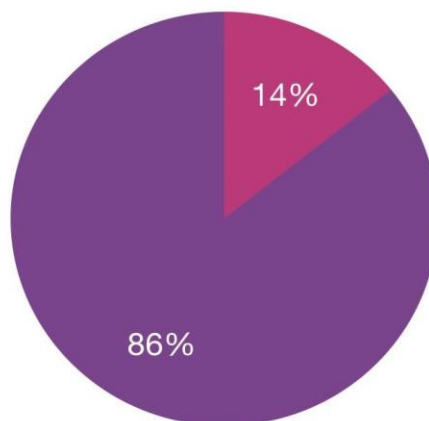


Figure 2: Pie Chart showing the with male associated with lactobacillus infection and female associated with lactobacillus infection. Male 14% represent in pink colour and female (86%) represent in violet colour .

DISCUSSION

In line with previous studies this study also showed high prevalence (6.9%) of UTI among DM patients. DM have various impairments in the immune system (low urinary concentration of interleukin-8 and interleukin-6, lower urinary leukocyte cell count), poor metabolic control and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of UTIs in DM patients. (Berezowsky *et al.*, 2021) Similar patterns of UTIs were observed in previous studies done by (Mulvey, Klumpp and Stapleton, 2020)(38%) and (Mulvey, Klumpp and Stapleton, 2020; Dobrek, 2021)(37%) and (Sewify *et al.*, 2016)(35%). Whereas, there was high prevalence of UTI reported by (Ding *et al.*, no date; Sewify *et al.*, 2016)(51%), (62%). Few studies found less prevalence of UTI than this study. These studies include Gillani *et al.* (29.2%), (Siddiqui *et al.*, 2020)(25.2%) and (Almukhtar, 2018)(19.5%).

In terms of gender, females are more infected in UTI than males. Women are more prone to UTIs due to their anatomy and reproductive system. Short urethra, urethra closer to the perirectal area where pathogen colonies are easier, absence of bacteriostatic prostatic secretions and sexual intercourse may force bacteria into the female bladder which can cause UTI infection. In line with previous studies, this study results also showed higher prevalence of UTI among females compared to males.

Prevalence among elderly and non-elderly was nearly equal with slightly higher in non-elderly patients. In women there are high chances of UTI infection in child bearing age that could be due to sexual intercourse and use of contraception (e.g. diaphragm and spermicides). Whereas in elderly patients loss of estrogen causes a change in the vaginal flora, loss of lactobacilli in the vaginal flora results in periurethral colonization. Decreased bladder capacity and increased urine production,

Most of the UTI cases were found to be poor glycaemic control. Poor metabolic control may suppress the immune system. Furthermore, high urine glucose concentration shows significant bacterial growth than normal urine. High concentration of sugar in urine may act as good media for the growth of uropathogen. Similarly other studies also stated the high prevalence of UTI in patients with uncontrolled DM

CONCLUSION

In the current study it is found that lactobacilli infections are more common in diabetic patients. As this study is conducted among diabetic patients, the factors contributing in this study are multiple, which are commonly seen in the diabetic patients. Lactobacilli infections should be considered as an indicator of the poor resistance in their body and susceptible for any infections. It is recently found in COVID 19 patients.

It is necessary to examine the patients reporting UTI symptoms in order to gain a better understanding and knowledge about UTI. Attention must be paid to potential predisposition which can work as factors favoring reinfection, because they disturb the normal

storage-voiding cycle or reduce body defenses. In particular, any neurologic condition must be taken into account, along with metabolic dysfunction (eg, diabetes), gynecological disorders, and known infectious diseases.

ACKNOWLEDGMENTS

We would like to thank Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University for providing us with the support to conduct the study.

CONFLICT OF INTEREST

The author declares that there were no conflicts of interests in the present study.

CONTRIBUTORS

M.V shreejha, principle investigator, Muralidharan N.P study designing, guidance and analysis of the results and interpretation.

SOURCE OF FUNDING

The present project is supported by

- Saveetha Institute of Medical and Technical Sciences
- Saveetha Dental College and Hospitals, Saveetha University
- LIC

REFERENCES

1. Almkhtar, S. H. (2018) 'Urinary Tract Infection Among Women Aged (18-40) Years Old in Kirkuk City, Iraq', *The Open Nursing Journal*, pp. 248–254. doi: 10.2174/1874434601812010248.
2. Barma, M. D. et al. (2021) 'Inhibition of *Streptococcus mutans*, antioxidant property and cytotoxicity of novel nano-zinc oxide varnish', *Archives of oral biology*, 126, p. 105132.
3. Berezowsky, A. et al. (2021) 'Glucose tolerance test with a single abnormal value in pregnancy and the risk of type-2 diabetes mellitus', *Archives of gynecology and obstetrics*. doi: 10.1007/s00404-021-06207-3.
4. Chee Wei Tan, M. P. C. (2016) 'Urinary tract infections in adults', *Singapore medical journal*, 57(9), p. 485.
5. Ding, D. et al. (no date) 'Comparison of balloon dilation tract real-time monitored by ultrasound combined with endoscopic versus unitary ultrasound guided in percutaneous nephrolithotomy: a retrospective study'. doi: 10.21203/rs.3.rs-618405/v1.
6. Dobrek, Ł. (2021) 'DRUG-RELATED URINARY TRACT INFECTIONS', *Wiadomosci lekarskie*, 74(7), pp. 1728–1736.
7. Flores-Mireles, A. L. et al. (2015) 'Urinary tract infections: epidemiology, mechanisms of infection and treatment options', *Nature reviews. Microbiology*, 13(5), pp. 269–284.
8. Geerlings, S. E. (2008) 'Urinary tract infections in patients with diabetes mellitus:
9. epidemiology, pathogenesis and treatment', *International Journal of Antimicrobial Agents*, pp. 54–57. doi: 10.1016/j.ijantimicag.2007.07.042.
10. Gelotar, D. P. et al. (2012) 'Candida Urinary Tract Infection (UTI) in Paediatric Population in Jamnagar District', *International Journal of Scientific Research*, pp. 153–154. doi: 10.15373/22778179/nov2012/53.
11. Girija, A. S. (2021) 'Fox3 (+) CD25 (+) CD4 (+) T-regulatory cells may transform the nCoV's final destiny to CNS! COMMENT'. WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.
12. Girija, A. S. S., Shankar, E. M. and Larsson, M. (2020) 'Could SARS-CoV-2-Induced
13. Hyperinflammation Magnify the Severity of Coronavirus Disease (CoViD-19) Leading to Acute Respiratory Distress Syndrome?', *Frontiers in immunology*, p. 1206.
14. Hoepelman, A. I. M. (no date) 'PATHOGENESIS AND MANAGEMENT OF BACTERIAL URINARY TRACT INFECTIONS IN ADULT PATIENTS WITH DIABETES MELLITUS',
15. *The Kidney and Hypertension in Diabetes Mellitus*, pp. 223–240. doi: 10.4324/9780203326916_chapter_14.
16. Iswarya Jaisankar, A. et al. (2020) 'Molecular characterisation of *csgA* gene among ESBL strains of *A. baumannii* and targeting with essential oil compounds from *Azadirachta indica*', *Journal of King Saud University - Science*, 32(8), pp. 3380–3387.
17. Jayaseelan, V. P. and Arumugam, P. (2020) 'Exosomal microRNAs as a promising theragnostic tool for essential hypertension', *Hypertension research: official journal of the Japanese Society of Hypertension*, 43(1), pp. 74–75.
18. Jayaseelan, V. P. and Paramasivam, A. (2020) 'Emerging role of NET inhibitors in
19. cardiovascular diseases', *Hypertension research: official journal of the Japanese Society of Hypertension*, 43(12), pp. 1459–1461.
20. Kumar, S. P., Girija, A. S. S. and Priyadharsini, J. V. (2020) 'Targeting NM23-H1-mediated inhibition of tumour metastasis in viral hepatitis with bioactive compounds from *Ganoderma lucidum*: A computational study', *Indian Journal of Pharmaceutical Sciences*, 82(2). doi: 10.36468/pharmaceutical-sciences.650.

21. Mathivadani, V., Smiline, A. S. and Priyadharsini, J. V. (2020) 'Targeting Epstein-Barr virus nuclear antigen 1 (EBNA-1) with *Murraya koengii* bio-compounds: An in-silico approach', *Acta virologica*, 64(1), pp. 93–99.
22. Medina, M. and Castillo-Pino, E. (2019) 'An introduction to the epidemiology and burden of urinary tract infections', *Therapeutic advances in urology*, 11, p. 1756287219832172.
23. Mody, L. and Juthani-Mehta, M. (2014) 'Urinary tract infections in older women: a clinical review', *JAMA: the journal of the American Medical Association*, 311(8), pp. 844–854.
24. Mulvey, M. A., Klumpp, D. J. and Stapleton, A. E. (2020) *Urinary Tract Infections: Molecular Pathogenesis and Clinical Management*. John Wiley & Sons.
25. Nitzan, O. et al. (2015) 'Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management', *Diabetes, metabolic syndrome and obesity: targets and therapy*, 8, pp. 129–136.
26. Paramasivam, A., Priyadharsini, J. V. and Raghunandhakumar, S. (2020) 'Implications of m6A modification in autoimmune disorders', *Cellular & molecular immunology*, 17(5), pp. 550–551.
27. Paramasivam, A. and Vijayashree Priyadharsini, J. (2020) 'Novel insights into m6A modification in circular RNA and implications for immunity', *Cellular & molecular immunology*, 17(6), pp. 668–669.
28. Paramasivam, A., Vijayashree Priyadharsini, J. and Raghunandhakumar, S. (2020)
29. 'N6-adenosine methylation (m6A): a promising new molecular target in hypertension and cardiovascular diseases', *Hypertension research: official journal of the Japanese Society of Hypertension*, 43(2), pp. 153–154.
30. Priyadharsini, J. V. et al. (2018) 'In silico analysis of virulence genes in an emerging dental pathogen *A. baumannii* and related species', *Archives of Oral Biology*, pp. 93–98. doi: 10.1016/j.archoralbio.2018.07.001.
31. Ramalingam, A. K., Selvi, S. G. A. and Jayaseelan, V. P. (2019) 'Targeting prolyl tripeptidyl peptidase from *Porphyromonas gingivalis* with the bioactive compounds from *Rosmarinus officinalis*', *Asian biomedicine: research, reviews and news*, 13(5), pp. 197–203.
32. Reddy, P. et al. (2020) 'Dental Caries Profile and Associated Risk Factors Among Adolescent School Children in an Urban South-Indian City', *Oral health & preventive dentistry*, 18(1), pp. 379–386.
33. Saliba, W. et al. (2015) 'Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management', *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, p. 129. doi: 10.2147/dmso.s51792.
34. Samuel, S. R. (2021) 'Can 5-year-olds sensibly self-report the impact of developmental enamel defects on their quality of life?', *International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children*, 31(2), pp. 285–286.
35. Samuel, S. R. et al. (2021) 'Dental pain, parental SARS-CoV-2 fear and distress on quality of life of 2 to 6 year-old children during COVID-19', *International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children*, 31(3), pp. 436–441.
36. Sewify, M. et al. (2016) 'Prevalence of Urinary Tract Infection and Antimicrobial Susceptibility among Diabetic Patients with Controlled and Uncontrolled Glycemia in Kuwait', *Journal of diabetes research*, 2016, p. 6573215.
37. Siddiqui, K. et al. (2020) 'Association of urinary non-albumin protein with the different urinary marker for glomerular and tubular damage in patients with type 2 diabetes', *BMC Nephrology*. doi: 10.1186/s12882-020-01906-6.
38. Teja, K. V. and Ramesh, S. (2020) 'Is a filled lateral canal - A sign of superiority?', *Journal of dental sciences*, 15(4), pp. 562–563.

39. Ushanthika, T. et al. (2021) 'An in silico approach towards identification of virulence factors in red complex pathogens targeted by reserpine', *Natural product research*, 35(11), pp. 1893–1898.
40. Vijayashree Priyadharsini, J. (2019) 'In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens', *Journal of periodontology*, 90(12), pp. 1441–1448.
41. Vijayashree Priyadharsini, J., Smiline Girija, A. S. and Paramasivam, A. (2018) 'An insight into the emergence of *Acinetobacter baumannii* as an oro-dental pathogen and its drug resistance gene profile - An in silico approach', *Heliyon*, 4(12), p. e01051.