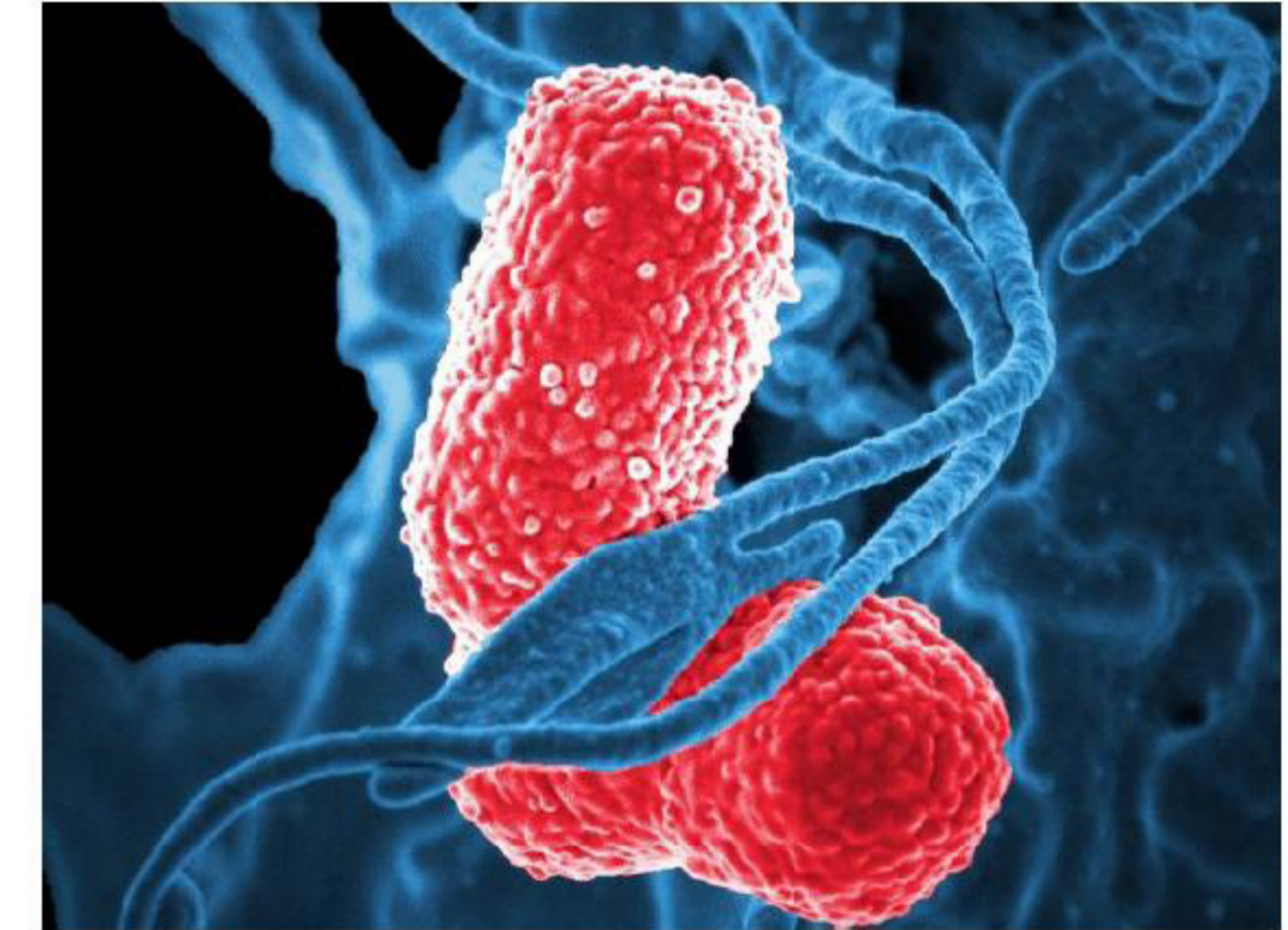


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Introduction: Urinary tract infections (UTIs) are common complications in renal transplant (RTx) recipients with prevalence up to 60% during the first year post-transplant. *Klebsiella pneumoniae* belong to Gram-negative, facultative anaerobic, nonmotile and nonflagellated bacilli. These are commensal bacteria of the nasopharynx and gastrointestinal tract. The latter is often the latent source for infections. *Klebsiella pneumoniae* with the most often isolated pathogen *Klebsiella pneumoniae* is a well recognized source of nosocomial infections in immunocompromised patients and is also the most common pathogen capable of producing extended-spectrum β -lactamases (ESBL). *Klebsiella pneumoniae* is also the most common pathogen in recurrent UTIs during first year after RTx. What is more, it is the second most common Gram-negative causative agent of bloodstream infections in solid organ transplant recipients. Due to multidrug resistance *Klebsiella pneumoniae* upper UTIs are serious, even life-threatening problem. Therefore the aim of the study was to assess both host and pathogen-related risk factors for developing *Klebsiella pneumoniae* upper UTIs.



Patients and methods: We analyzed *Klebsiella pneumoniae* isolates from RTx patients who are followed up at Gdańsk Transplantation Centre with reference to clinical data. The following variables were considered: etiology of end-stage renal disease, age, sex, comorbidity (estimated with the use of Charlson Comorbidity Index (CCI)), recurrent UTIs before RTx, dialysis type, pretransplant dialysis time, repeated transplantation, episodes of acute rejection (AR), acute tubular necrosis (ATN), delayed graft function (DGF), use of a double-J ureteral stent, type of immunosuppression used (cyclosporine, tacrolimus, everolimus, mycophenolate mofetil/sodium), induction therapy with monoclonal (basiliximab) and polyclonal antibodies (antithymocyte globulin ATG), CMV infections. Multiplex PCR was used to investigate the presence of the following virulence genes: fimH-1, uge, irp-2, kpn, mrkD, ycfM. The virulence profile was compared with that of isolates from non-RTx patients.

Statistical analysis

All analyses were performed using Statistica 12.0 (StatSoft) software. Two-tailed Student's unpaired t test or Mann-Whitney's test were used to compare continuous variables and the χ^2 or Fischer exact test were used to compare proportions, as appropriate. All tests were two-sided. $P \leq 0,05$ was considered to be statistically significant.

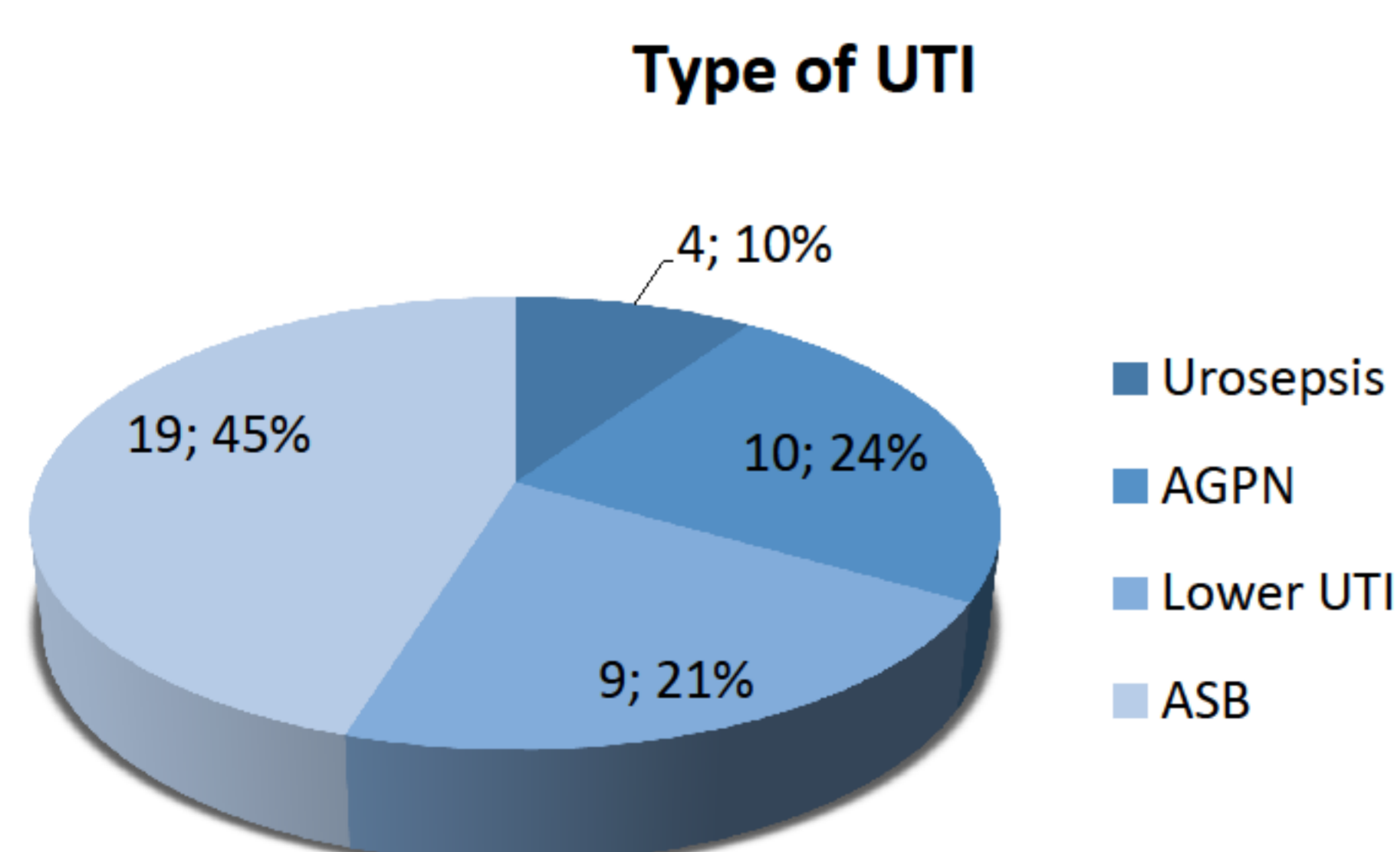
Characteristics of the selected virulence factors

fimH-1	gene encoding mannose-specific adhesin subunit of type 1 fimbriae Type 1 fimbriae, and the adhesive subunit FimH in particular, play an important role in UTI caused by <i>K. pneumoniae</i> and is involved in biofilm formation
uge	gene encoding uridine diphosphate galacturonate 4-epimerase essential for capsule and smooth lipopolysaccharide synthesis
irp-2	siderophore; promotes biofilm formation under iron-depleted conditions
kpn	FimH-like adhesin
mrkD	gene encoding mannose-specific adhesin subunit of type 3 fimbriae Type 3 fimbriae allow adhesion to various human tissue structures (kidney, lung, bladder) and are potent promoter of biofilm formation on biotic and abiotic surfaces
ycfM	outer membrane lipoprotein

The prevalence of *Klebsiella pneumoniae* virulence factors in RTx and non RTx patients

	RTx patients (n=42)	Non-RTx patients (n=15)	p
fimH-1	31 (76,2%)	13 (86,7%)	0,48
uge	36 (85,7%)	13 (86,7%)	1,0
irp-2	19 (45,2%)	6 (40%)	0,77
kpn	30 (71,4%)	13 (86,7%)	0,31
mrkD	38 (90,5%)	13 (86,7%)	0,65
ycfM	35 (83,3%)	13 (86,7%)	1,0

Results:



- 83% of UTI episodes were due to ESBL+ strains, while there were no carbapenemase producing strains.
- Vesico-ureteral reflux or strictures at the uretero-vesical junction and lower urinary tract malformation as underlying cause of CKD emerged as independent predictors of *Klebsiella pneumoniae* upper UTIs
- We found no association between virulence factors profile and the type of UTI (lower UTI vs. upper UTI)
- The prevalence of **uge** gene was significantly lower in RTx patients on **everolimus** based immunosuppression when compared to isolates from patients not receiving mTOR inhibitors (89,7% vs 33,3% $p < 0,05$).
- **irp-2 – versiniabactin**, was significantly more common in RTx patients who received **basiliximab** when compared to no-induction protocols (69,2% vs 34,5% $p = 0,04$).

Conclusions: *Klebsiella pneumoniae* upper UTI may be a marker of urine flow impairment e.g. vesico-ureteral reflux or strictures at the uretero-vesical junction. Type or strength of immunosuppression used may influence the selection of strains with particular virulence factor profile.