RESEARCH ARTICLE

Uroflowmetry: nomograms in healthy young Pakistani men

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Abstract

Objective: To create a nomogram based on urine volume and flow of males without lower urinary tract symptoms.

Method: The prospective, cross-sectional study was conducted at the Department of Urological Surgery and Transplantation, Jinnah Postgraduate Medical Centre, Karachi, from November 1, 2020, to October 31, 2022, and comprised healthy young males without lower urinary tract dysfunction who were recruited from the hospital as well as a large textile mill. They were asked to void on their normal desire. Uroflowmetry was done to determine maximum flow rate, average flow rate, and void volume values. A best-fit regression model was used to formulate uroflowmetry nomogram using average and maximum urine flow rate over voided volume. The sample size was calculated using PASS 2020 Power Analysis and Sample Size Software (2020). NCSS, LLC. Kaysville, Utah, USA. The database was developed on NCSS 2020 Statistical Software (2020). NCSS, LLC. Kaysville, Utah, USA for the data analysis.

Results: Of the 468 male subjects enrolled, data was analysed related to 432(92.3%). The mean age was 25.59±4.32 years. Mean maximum flow rate, average flow rate and void volume were 25.28±8.70mL/s, 14.77±4.79mL/s and 405.48±163.86mL, respectively. The association of age was noted with maximum flow rate ($r=0.1435$, $p=0.004$), average flow rate ($r=0.1135$, $p=0.004$) and void volume ($r=0.0619$, $p=0.004$). The best-fitted model for maximum and average flow rate was subsequently developed which was statistically significant ($p<0.05$).

Conclusion: The nomograms developed could reliably predict the maximal flow rate in young Pakistani men.

Key Words: Nomogram, Maximum flow rate, Lower urinary tract symptoms, Pakistan.

(JPMA 74: 1806; 2024) **DOI: https://doi.org/10.47391/JPMA.10626**

Introduction

Uroflowmetry (UFM), one of the most extensively utilised screening tool[1], is a non-invasive urodynamic test that estimates the flow rate of urine during voiding. UFM has a multitude of features, but the key parameters are the maximum flow rate (Qmax), average flow rate (Qave) and void volume (VV)[2], among which the most significant is Qmax. Although not life-threatening, the quality of life (QOL) is significantly affected in patients with symptoms of voiding dysfunction[3]. In patients with lower urinary tract symptoms (LUTS), evaluation of the LUT integrity, both pre- and post-therapy, and follow-up are made easier by the determination of peak flow rate. Numerous variables, such as VV, psychological inhibition, abdominal strain, etc., have an impact on flow rates.[4]

The first modern uroflow metre was developed in 1946 by Willard Drake[5]. To predict the UFM results in each patient population, several nomograms have been developed to ascertain the relationship between flow rate and VV, but most of them have limitations. The first nomogram was created in 1973[6] by Susset et al. and it was modified in 1979 by Siroky et al.,[7] which, in contrast to other nomograms, incorporated the bladder volume (VV plus residual volume [RV]). The study concluded that such an approach would enable more insightful evaluation of changes in urine flow rate following medical or surgical treatment as well as better separation between healthy and obstructed patients.[7] Haylen at al. developed the Liverpool nomogram in England using data from 331 males without voiding dysfunction, and 1 flow per participant[8]. The average age of the participants was 49 years (range: 16-64 years). The Qmax in the study declined with advancing age (1.0-1.6mL/s per 10 years of age). Unlike bladder volume, VV was accounted for in the Liverpool nomogram[8]. Uroflowmetry analysis frequently employs both Liverpool and Siroky nomograms. In 2019, a research comparing the two nomograms was carried out[9]. The Liverpool nomogram identified a pathological uroflowmetry in one-third of the participants who did not report having LUTS and had normal uroflowmetry on the Siroky nomogram. A significant discrepancy was observed between the two nomograms, and the study concluded that the two most popular UFM nomograms had very low concordance with one another[9].

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Submission complete: 11-08-2023 **Review began:** 13-10-2023

Acceptance: 03-08-2024 **Review end:** 20-04-2024

Discrepancies in a variety of normal as well as disease parameters can be attributed to racial and ethnic disparities[10-12]. Currently available nomograms occasionally differ significantly as flow rates may differ depending on demographics.

The current study was planned to create a nomogram based on urine volume and flow of Pakistani males without LUTS.

Subjects and Methods

The prospective, cross-sectional study was conducted at the Department of Urological Surgery and Transplantation, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from November 1, 2020, to October 31, 2022. After approval from the institutional ethics review board, a pilot study was conducted to estimate the mean values of Qave and Qmax before determining the sample size. An effect size of 0.15 was estimated[13] to calculate the sample size with 99% power to reject the null hypothesis of zero effect size when the population effect size is 0.15 and the significance level (alpha) is 0.050 using a two-sided one-sample t-test. Considering a dropout rate of 20%, the sample size was inflated[14].

The sample comprised healthy young males aged 15-40 years without LUT dysfunction who were recruited from JPMC as well as a large textile mill. The subjects had no known urological, neurological or psychological disease, no history of any congenital anomaly, such as hypospadias or meatal stenosis, and no history of catheterisation. Individuals who were known to have diabetes, had a history of neurological disorders, psychological disorders, urological disorders, such as LUTS, infections, LUT stones or malignancy, meatal stenosis, etc., and those who were on medical therapy that adversely impacted the function of the LUT, such as 5-alpha reductase inhibitors, anticholinergics, and alpha-blockers, were excluded.

After taking informed consent from the subjects, standardised UFM was performed using a UFM device (DanFlow 3000 Plus, MEDKONSULT, device name), which converts patient urine flow into a graphical representation using weight cell transducer technology. The device was calibrated at the JPMC and the textile mill. The statistics typically required included Qave, Qmax, VV, and flow time. The UFM was administered when the subjects experienced the desired sensation of a full bladder. Only representative continuous voids with a volume of at least 150ml were included. The participants were instructed to empty their bladders into special containers attached to the UFM device, and the association involving VV, Qmax and Qave was studied.

A specific reference interval for VV using the method of two-sided 95% percentile was calculated to truncate unusually high or low VV values. The data analysed ranged 151.8-794.4mL.

The sample size was calculated using PASS 2020 Power Analysis and Sample Size Software (2020). NCSS, LLC. Kaysville, Utah, USA[14]. The database was developed on Number Cruncher Statistical Systems (NCSS) 2020 Statistical Software (2020). NCSS, LLC. Kaysville, Utah, USA for the data analysis[14]. Pearson Correlation coefficients (r) were calculated for age (years), VV (mL), Qmax (mL/s), and Qave (mL/s) to determine the degree of association among the variables. Specific reference interval for VV was calculated through Statistical Software (2020). NCSS, LLC. Kaysville, Utah, USA. This procedure estimates a reference interval for cross-sectional studies using the methodology of Altman (1993), Royston and Wright (1998), and Royston and Sauerbrei (2008)[15]. The middle 95% reference interval for the VV was also calculated for an accurate interval. Simple linear regression analysis was performed for Qmax and Qave as dependent variables (Y-axis) and VV as independent variable (X-axis) to assess the coefficient of determination (R^2) before adjusting for the best-fitted model. The best-fit regression models were searched for the predictions of Qmax and Qavg with the maximum R^2.

Results

Of the 468 male subjects enrolled, data was analysed related to 432(92.3%). The mean age was 25.59±4.32 years. Mean Qmax, Qave and VV were 25.28±8.70mL/s, 14.77±4.79mL/s and 405.48±163.86mL, respectively. The association of age was noted with Qmax (r=0.1435, p=0.004), Qave (r=0.1135, p=0.004) and VV (r=0.0619, p=0.004).

Age was poorly associated with UFM variables (p=0.004 is relevant to Pearson's correlation coefficient r=0.1435 and r=0.1135 which authenticated the poor interrelationship of age with Qmax., Qave., and VV).

Simple linear regression analysis was performed to determine the relationship involving Qmax, Qave and VV without any adjustment to the data (Figures 1-2): Qmax = 18.229 + 0.01739 × VV (R2=0.1073, p=0.001), and Qave = 10.869 + 0.00963 × VV (R2=0.1083, p=0.001).

Due to very low correlation of determination (R2) between Qmax (0.1073) and Qave (0.1083) with VV, the variable of VV was transformed into polynomial variable (x3) and natural logarithms LN(x) for attaining the maximum value of R2by using the best-fit model as:

Qmax = 20.2578 + (6.396×10-7) × (VV)3 - (9.339×10-8) ×

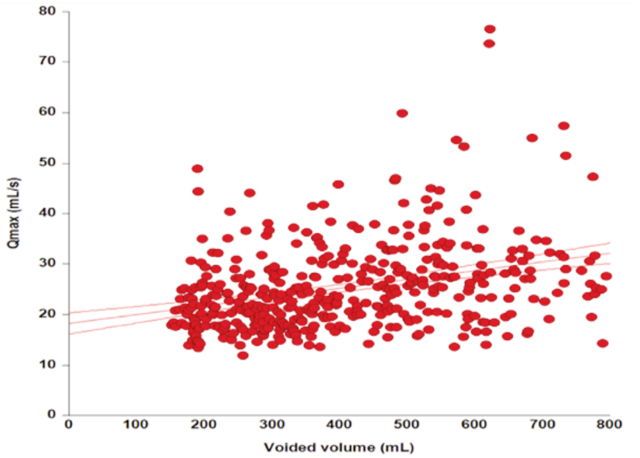

Figure-1: Association of Qmax (mL/s) with VV (mL) before adjustment for VV (Qmax [mL/s]= (18.22) + [0.01739] * VV [mL], R2=0.1073, p=0.001).
Qmax: Maximum flow rate, VV: Void volume.

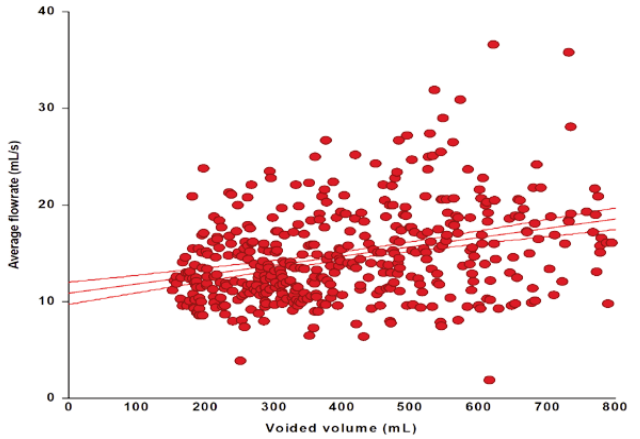

Figure-2: Association of Qave (mL/s) with VV (mL) before adjustment for VV (Qave [mL/s]= 10.87 + 0.0096 * VV [mL] R^2=0.1083, p=0.001).
Qave: Average flow rate, VV: Void volume.

LN (VV) × (VV)3 (R2=0.9444, p=0.001), and Qave = 12.1338 + (3.218×10-7) × (VV)3 - (4.679×10-8) × LN (VV) × (VV)3 (R2=0.9621, p=0.001).

The validity of the adjustment through the VV-specific reference interval, and the value of R2 for the full model were calculated for Qmax (R2=0.9444, p=0.001) and Qave

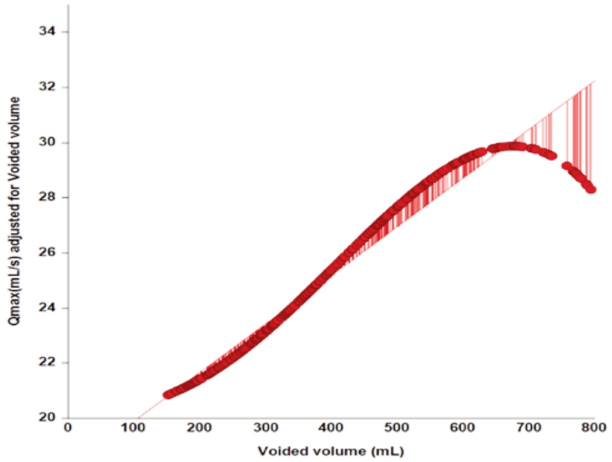

Figure-3: Final model derived for prediction of Qmax (mL/s) on the basis of VV (mL^3).
Predicted Qmax (mL/s) = 20.2578 + (6.396×10-7) × (VV mL)3 - (9.339×10-8) × LN (VV mL) × $(VV\ mL)^3$, R^2 = 0.9444, p = 0.001.
Qmax: Maximum flow rate, VV: Void volume.

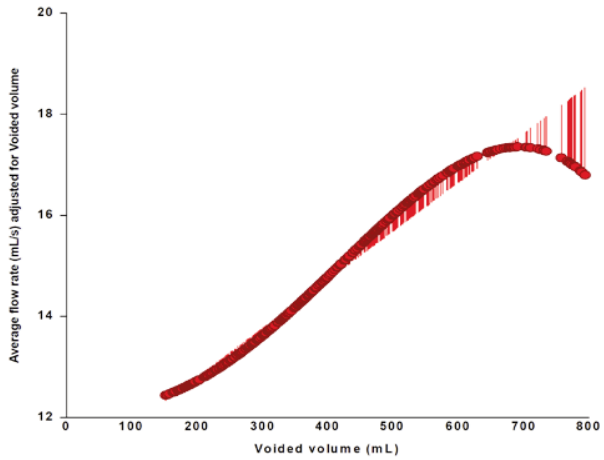

Figure-4: Final model derived for prediction of Qave (mL/s) on the basis of VV (mL^3).
Predicted Qave (mL/s) = 12.1338 + (3.218×10-7) × (VV mL)3 - (4.679×10-8) × LN (VV mL) × $(VV\ mL)^3$, R^2 = 0.9621, p = 0.001.
Qave: Average flow rate, VV: Void volume.

(R2=0.9621, p=0.001).

Qmax = 18.229 + 0.01739 × VV (R2=0.9444, p=0.001), and Qave = 10.869 + 0.00963 × VV (R2=0.9621, p=0.001)

After confirmation of a significant increase in R2, the best-fit regression model for the prediction of Qmax and Qave were selected (Figures 3-4), which were: Predicted Qmax = 20.2578 + (6.396×10-7) × (VV)3 - (9.339×10-8) × LN (VV) × (VV)3 (R2=0.9444,

Table-1: Validation of the best-fitted model.

Variables	Estimated through best fitted model	Values through Uroflowmetry	Mean difference	p-value
Qmax (mL/sec) (n=30)	21.57 ± 6.43	23.72 ± 2.65	2.144 ± 6.43	0.083
Qave (mL/sec) (n=30)	13.13 ± 4.26	13.95 ± 1.43	0.81 ± 4.51	0.339

Qmax: Maximum flow rate, Qave: Average flow rate.

p=0.001), and Predicted Qave = 12.1338 + (3.218×10-7) × (VV)3 - (4.679×10-8) × LN (VV) × (VV)3 (R2=0.9621, p=0.001).

The best-fit models for both Qmax and Qave were re-validated for a further 30 UFM measurements that were not included in the study to determine the difference, on average, between estimated values through the prediction model and those computed through UFM. The mean difference was statistically non-significant (Table).

Discussion

UFM is a frequently used investigation in the preliminary diagnosis of LUT dysfunction, and it also serves as an important follow-up technique. The characteristics of bladder contraction and urethral resistance determine the UFM parameters[16]. To achieve normal reference values for flow rates over various urine volumes, a number of nomograms have been designed and assessed. In the current study, an innovative standard-deviation-based nomogram of VV and flow was successfully developed using information collected from a significant proportion of Pakistani males without LUTS. A statistical reference interval technique was employed to attain boundaries for UFM variables in their development to surmount the challenges posed by extreme values when untrimmed data was used.

Different ethnicities and/or ages may result in varied urine flow. In Canadian[7] and Liverpool nomograms[8], the mean Qmax was approximately 30mL/s at approximately 400mL, but in the current study at approximately 405.48ml, it was almost 25.28ml/s. The same was observed in a Japanese study, where the mean Qmax was 25ml/s at VV 400ml[17]. In a study with participants aged 15-40 years, the mean Qmax was 24.32±3.50 at VV 420.93±97.89ml18. The same study also reported a negative but significant association between Qmax and age (r=0.21, p<0.0001)18. The current study, however, demonstrated that among patients of similar age groups, Qmax and Qave was poorly associated with age (r=0.1435 and r=0.1135). Therefore, the current nomogram may be the most efficacious nomogram for screening voiding dysfunction in Pakistani males aged ≤40 years.

The coefficient of determination for Qmax and Qave with VV as a highly predicted model (R2=0.9444, p=0.001 for Qmax, and R2=0.9621, p=0.001 for Qave), showed that the greater the VV, the higher were the flow rates. This was also seen in other investigations[7,8]. However, this increase in volume is acceptable to a certain extent. In the current study, as VV exceeded 794ml, the connection between Qmax and VV plateaued and started to deteriorate. Many investigations observed a linear rise in Qmax up to 700ml followed by a plateau[19]. One explanation might be that detrusor contraction weakens when the bladder is over-distended[20]. In a study, the mean values for Qmax and VV obtained from participants with normal desire to void versus strong desire to void were 17.5±6.8 and 19.7±7.7 mL/sec (p<0.0001) for Qmax, and 207±104 and 369±168mL (p<0.0001) for VV, respectively. Compared to the group with a regular urge to void, all metrics were significantly higher in the group with a strong desire to void or urgency[21]. In the current study, individuals were asked to void whenever they experienced a normal urge to void, which is acceptable globally.

The current study has certain limitations. In a bid to replicate normal behaviour in the event of a pathological void, repeated evaluation is required[22], but the current study only recorded one uroflow reading. Also, the sample size and age group could have been increased.

Conclusion

The nomogram developed could reliably predict Qmax by VV in Pakistani adult males aged 15-40 years. Accurate evaluation of UFM results is important given that it serves as the foundational initial study in the management of voiding disorders. Flow-volume nomograms created for the Caucasian population are currently not ideally applicable to the Asian population.

Acknowledgement: The study was carried out in collaboration with the LUTS Research Group, Pakistan. We are grateful to Mr Muhammad Akhtar Anwer for statistical analysis and data presentation.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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Authors' Contribution:
MAS: Study design, concept, questionnaire design, data collection and review.
SA: Study design, concept, questionnaire design, data collection, drafting and review.
AK: Literature search, data analysis, interpretation and drafting.