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Development of Uroflowmetry Nomograms for Healthy Young Pakistani Men

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Author`s Contribution

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ABSTRACT

Objective: To develop age-specific uroflowmetry nomograms and percentile reference values for Qmax, Qave, voided volume and voiding time in healthy Pakistani men aged 20–40 years.

Methodology: A descriptive cross-sectional study was conducted in the Department of Urology at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, from March 2024 to September 2024. Through non-probability consecutive sampling, 200 young men within the age group of 20-40 years, with IPSS score of ≤7, free of any urological disease, having normal digital rectal examination, and voided volume ≥150 ml were selected. Uroflowmetry test was done using the calibrated Dantec Menuet uroflowmeter. The age-specific percentile values were calculated and represented graphically.

Results: From 218 men recruited for testing, 200 were enrolled. The average age of participants was 29.4±5.8 years, while the average body mass index was 24.1±3.2 kg/m2. The mean value of Qmax among these subjects was 22.6±4.3 ml/sec; the average Qave was 11.8±2.6 ml/s; voided volume, 318.4±72.1 ml; and voiding time, 28.7±7.4 sec. The value of Qmax at the 50th percentile decreased steadily from 25.1 ml/sec among those aged 20–24 years to 20.4 ml/sec among those aged 35–40 years. The correlation between Qmax and age was significantly negative (r=-0.31, p<0.001). The values of Qmax among Pakistani men exceeded those predicted by the Liverpool nomogram by 12-18% at each age level (p<0.001).

Conclusion: This study developed age-specific uroflowmetry nomograms and percentile reference values for Qmax, Qave, voided volume, and voiding time in healthy young Pakistani men.

Keywords: Uroflowmetry, Nomogram, Maximum Flow Rate, Qmax, Lower Urinary Tract Symptoms, Bladder Outlet Obstruction.

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Introduction

Uroflowmetry remains the most frequently utilized screening method for evaluating urodynamics in non-invasive clinical urology, assessing the rate of voiding of urine from the bladder and generating objective evidence regarding lower urinary tract physiology in the absence of catheterization or intravascular instrumentation.[1] Of all the quantifiable variables in uroflowmetry tests, the maximum flow rate (Qmax) remains the most clinically relevant indicator, representing the main screening tool for assessing bladder obstruction and evaluating the efficacy of therapy in male patients with LUTS.[2] These indicators comprise Qmax, average flow rate (Qave), voided volume, and voiding duration and they differ across ages, genders, ethnic groups, and geographical regions, necessitating the development of population-based normative values.[3]

The clinical relevance of uroflowmetry tests depends entirely upon the accuracy of reference data based on specific populations. Otherwise, clinicians must make use of nomograms based on reference data obtained from populations with very different genetics, anatomy, dietary preferences, and lifestyles. The Liverpool nomogram was created by Haylen et al., based on a sample size of 331 healthy males in England.[4] The Siroky nomogram was

created in the USA. Both have been useful tools in clinical practices for many years, but recent findings in neighbouring South Asian countries have shown that there is considerable systematic bias in applying these nomograms in Pakistan. Several studies in India and Bangladesh have indicated that there are real physiological differences between South Asian men and the Western reference groups, with Qmax values and voiding volumes that fall well outside of the normal range.[5,6]

Pakistan, a country with a population of more than 240 million, does not yet have an established uroflowmetry reference database for its population. This gap poses a practical challenge for urologists in Pakistan, who may have to rely on Western nomograms or make clinical judgments in the absence of locally derived reference values. Such an approach may result in misclassification, unnecessary investigations, or even avoidable surgical interventions. With the increasing burden of lower urinary tract symptoms (LUTS) among Pakistani men, driven in part by an aging population, obesity, sedentary lifestyles, and changing dietary patterns, there is a growing need to establish reliable population-specific reference values against which uroflowmetry findings can be assessed.

Young adult men aged 20–40 years are particularly suitable for establishing such reference values because they are relatively less affected by age-related urological disorders. Several recent studies have reported that population-based nomograms can improve diagnostic accuracy compared with the use of international reference standards, with potential implications for patient safety and clinical decision-making.[7,8] Population-specific flow-volume nomograms have also demonstrated greater sensitivity and specificity than Caucasian-derived nomograms for detecting voiding dysfunction among South Asian men, further supporting the need for locally relevant reference standards rather than generalized international cutoffs.[9]

Therefore, the aim of this study was to develop age-based nomograms for uroflowmetry parameters in healthy Pakistani men aged 20–40 years and to establish percentile-based reference values (5th, 25th, 50th, 75th, and 95th percentiles) for maximum urinary flow rate (Qmax), average urinary flow rate (Qave), voided volume, and voiding time.

Methodology

This cross-sectional study was conducted at the Department of Urology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, over a six-month period from March 2024 to September 2024. Ethical approval was obtained from the Institutional Review Board of PIMS (Ref: PIMS/IRB/2024/113) and the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan. All study procedures were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant in either English or Urdu before any study-related procedure was performed.

The sample size was calculated using a sample size calculator for reference interval studies based on WHO criteria. An expected mean Qmax of 25 mL/s with a standard deviation of 6 mL/s in healthy young men was assumed, resulting in a coefficient of variation of 25%.[8] With a 95% confidence level and a 5% margin of error, and considering the WHO minimum requirement of 120 participants for determining a reference interval, the sample size was increased by 10% to account for potential losses and incomplete observations, resulting in a final target sample size of 200 participants.

Consecutive non-probability sampling was used. All eligible men presenting to the Department of Urology during the study period were enrolled until the required sample size was reached. Participants were eligible if they were Pakistani men aged 20–40 years, had an International Prostate Symptom Score (IPSS) of ≤7, had no previous history of urological disease or urological surgery, had a normal digital rectal examination, and were able to void at least 150 mL during uroflowmetry.

A normal digital rectal examination was defined as a prostate that was smooth, symmetrical, non-tender, and of normal consistency, with no palpable nodules or induration and no clinical features suggestive of benign prostatic enlargement or malignancy.

Participants were excluded if they had any pre-existing urological condition, including benign prostatic hyperplasia, prostatitis, urethral stricture, or neurogenic bladder; any neurological disorder that could affect voiding; were taking alpha-blockers, anticholinergic medications, or diuretics; had a urinary tract infection based on clinical assessment and urinalysis; had undergone urological instrumentation within the preceding four weeks; or had a post-void residual volume >100 mL on bladder ultrasonography.

Demographic information, including age, height, weight, body mass index (BMI), education, and occupation, was recorded on a structured proforma. All participants completed validated Urdu and English versions of the IPSS questionnaire. This was followed by a brief physical examination, including abdominal palpation and digital rectal examination to assess the prostate.

Participants were instructed to attend with a comfortably full bladder and to void in a soundproof room equipped with an electronic uroflowmeter (Dantec Menuet, Natus Medical, Denmark). The uroflowmeter continuously records urinary flow during voiding and generates a time-flow curve. The uroflowmeter was calibrated at the beginning of each clinical visit according to the manufacturer's instructions.

The following parameters were automatically recorded: maximum urinary flow rate (Qmax, mL/s), average urinary flow rate (Qave, mL/s), voided volume (mL), voiding time (seconds), time to maximum flow rate (seconds), and flow pattern. Flow patterns were classified as normal bell-shaped, interrupted, prolonged, or plateau.

Post-void residual (PVR) volume was measured immediately after voiding using a portable bladder ultrasound scanner (BladderScan BVI 9400, Verathon Inc., USA).

Data were coded and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables with a normal distribution were presented as mean ± standard deviation, while skewed variables were summarized as median and interquartile range. Normality was assessed using the Kolmogorov–Smirnov test. Categorical variables were presented as frequencies and percentages.

Participants were divided into four age groups: 20–24, 25–29, 30–34, and 35–40 years. The 5th, 25th, 50th, 75th, and 95th percentiles were calculated for each age group for the four uroflowmetry parameters. These percentile values were plotted against the midpoints of the respective age categories to develop nomogram curves using polynomial regression.

Pearson's correlation coefficient was used to assess correlations between normally distributed variables, whereas Spearman's rank correlation coefficient was used for skewed variables. Differences between groups were assessed using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc test for normally distributed variables. For skewed variables, the Kruskal–Wallis test followed by Dunn's post-hoc test was used.

Differences in Qmax at the 50th percentile between the nomogram developed in the present study and the Liverpool nomogram were assessed using a paired t-test for matching age and voided-volume strata. Independent predictors of Qmax were identified using multiple linear regression, with age, BMI, voided volume, and IPSS included as predictor variables.

Validation was performed using a 70:30 random split of the dataset into training and validation samples. Goodness of fit was assessed using the coefficient of determination (R^2). A p-value <0.05 was considered statistically significant.

Results

A total of 218 men were screened, of whom 200 met the eligibility criteria and were included in the final analysis. Eighteen participants were excluded because of elevated post-void residual volume (n=7), voided volume <150 mL (n=5), urinary tract infection (n=4), or alpha-blocker use (n=2). The mean age was 29.4±5.8 years and the mean BMI was 24.1±3.2 kg/m². The participants had a mean IPSS of 3.2±1.8 and mean post-void residual volume of 18.6±11.4 mL. A bell-shaped flow pattern was observed in 184 (92%) participants, while 12 (6%) had an interrupted pattern and 4(2%) had a plateau pattern (Table I).

Table I: Baseline Demographic and Clinical Characteristics of Participants. (n=200)

Variable	Value
Age, years (mean ± SD)	29.4 ± 5.8
Height, cm (mean ± SD)	171.2 ± 6.4
Weight, kg (mean ± SD)	70.6 ± 9.8
BMI, kg/m² (mean ± SD)	24.1 ± 3.2
IPSS score (mean ± SD)	3.2 ± 1.8
Post-void residual, ml (mean ± SD)	18.6 ± 11.4
Normal digital rectal examination, n (%)	200 (100%)
Normal bell-shaped flow pattern, n (%)	184 (92%)
Interrupted flow pattern, n (%)	12 (6%)
Plateau flow pattern, n (%)	4 (2%)
Education: Graduate or Post-graduate, n (%)	124 (62%)

The overall mean Qmax was 22.6±4.3 mL/s, Qave was 11.8±2.6 mL/s, voided volume was 318.4±72.1 mL, and voiding time was 28.7±7.4 seconds (Table II).

Qmax showed a progressive decline with increasing age (ANOVA $F=8.34$, $p<0.001$). The median Qmax decreased from 25.1 mL/s in men aged 20–24 years to 20.4 mL/s in those aged 35–40 years. The corresponding 5th percentile values were 16.8 and 12.6 mL/s,

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Table II: Overall Uroflowmetry Parameters for the Entire Cohort. (n=200)

Parameter	Mean ± SD	Median (IQR)	Range
Qmax (ml/s)	22.6 ± 4.3	22.4 (19.6–25.8)	12.1–36.4
Qave (ml/s)	11.8 ± 2.6	11.5 (9.8–13.6)	5.2–19.3
Voided Volume (ml)	318.4 ± 72.1	312 (268–368)	152–510
Voiding Time (s)	28.7 ± 7.4	28 (23–34)	12–58
Time to Qmax (s)	12.4 ± 4.1	12 (9–15)	4–28

Table III: Age-Specific Percentile Reference Values for Maximum Flow Rate — Qmax (ml/s)

Age Group (years)	N	5th	25th	50th	75th	95th
20–24	42	16.8	21.2	25.1	28.6	34.2
25–29	50	15.4	19.8	23.6	27.1	32.8
30–34	55	14.2	18.4	22.1	25.8	30.6
35–40	53	12.6	16.9	20.4	24.2	28.7

One-way ANOVA F=8.34, p<0.001. Post-hoc Tukey's test: 20–24 vs 35–40 years p<0.001; 25–29 vs 35–40 years p=0.004. All values in ml/s.

respectively, while the 95th percentile values were 34.2 and 28.7 mL/s (Table III; Figure 1). Significant differences were observed between the 20–24 and 35–40 year groups (p<0.001) and between the 25–29 and 35–40 year groups (p=0.004).

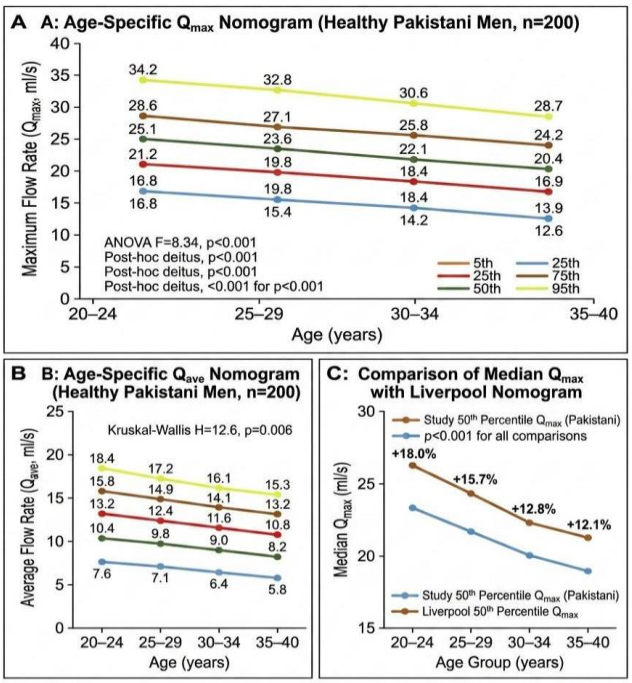


Figure 1: Age-specific nomogram curves and comparison with Liverpool norms for 200 healthy young Pakistani men. Panels A and B show Qmax and Qave nomograms with five percentiles, all showing a clear downward trajectory with increasing age. Panel C illustrates that the Pakistani 50th percentile Qmax curve is significantly displaced upwards compared to the corresponding Liverpool value across all age strata.

Qave also decreased significantly with age, with median values ranging from 13.2 mL/s in the youngest group to 10.8 mL/s in the oldest group (Kruskal–Wallis H=12.6, p=0.006) (Table IV). In contrast, voided volume did not differ significantly between age groups (p=0.25), whereas voiding time increased modestly with age, from 26.2±6.8 to 31.4±8.1 seconds (p=0.006).

Table IV: Age-Specific Percentile Reference Values for Average Flow Rate — Qave (ml/s)

Age Group (years)	n	5th	25th	50th	75th	95th
20–24	42	7.6	10.4	13.2	15.8	18.4
25–29	50	7.1	9.8	12.4	14.9	17.2
30–34	55	6.4	9.0	11.6	14.1	16.1
35–40	53	5.8	8.2	10.8	13.2	15.3

Kruskal-Wallis H=12.6, p=0.006 across age groups. All values in ml/s.

BMI had a weak negative correlation with Qmax (r=−0.14, p=0.046), whereas IPSS was not significantly associated with Qmax (r=−0.09, p=0.21). In multiple linear regression, voided volume was significantly associated with Qmax (β=0.042, 95% CI: 0.031–0.053; p<0.001), while age was not independently significant (β=−0.18, 95% CI: −0.44 to 0.08; p=0.18). The model explained 22.4% of the variance in Qmax (R^2=0.224, F=18.6, p<0.001).

Compared with the Liverpool nomogram at comparable voided volumes, the 50th percentile Qmax values in Pakistani men were higher across all age groups, with differences ranging from 12.1% to 18.0% (Figure 1). Internal validation using a 70:30 split produced an R^2 of 0.74 in the validation sample (n=60), with no systematic residual pattern.

The relationship between flow rates and voided volume is illustrated in Figure 2. Both Qmax and Qave showed an overall increase with increasing voided volume, with voided volume demonstrating a significant positive association with Qmax (r=0.38, p<0.001).

Discussion

To date, the first uroflowmetry nomograms based on age-stratification of Qmax for healthy young men in Pakistan

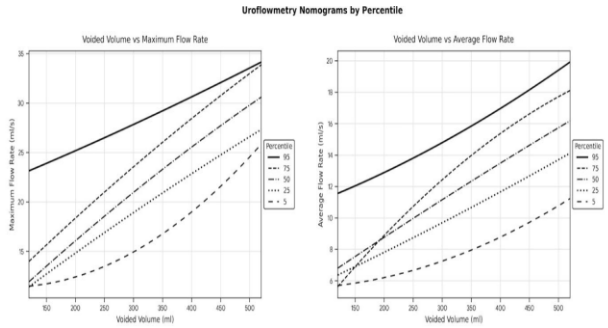


Figure 2: Uroflowmetry nomograms demonstrating the 5th, 25th, 50th, 75th, and 95th percentiles for Maximum Flow Rate (Qmax) (A) and Average Flow Rate (Qave) (B) against voided volume in healthy males.

have been proposed in this study, which aims to fill an important lacuna in South Asian urological reference standards. The most important clinical observation made is that healthy young Pakistani men show significantly higher Qmax scores at equivalent ages and voided volumes compared to predictions made by Liverpool nomogram, i.e. 12-18% higher ($p<0.05$ for all age groups), an important finding with practical implications in the clinical diagnosis of Pakistani urological patients.

The mean Qmax measured in this group, i.e. 22.6±4.3 ml/s falls within a similar range seen recently in other similar South Asian and middle-eastern cohorts, namely, 23.4 ml/s in a South Indian population with strict inclusion criteria and 22.1 ml/s in a middle-eastern country population with no urological voiding complaints.[6,10,11] The similarity between South Asian countries in terms of mean Qmax, ranging around 22-24 ml/s, compared with a significantly lower value found in western countries, i.e. 19-21 ml/s, indicates the presence of physiological variance, rather than a methodological artefact.[12] This could be due to various factors including different body composition, dietary habits, fluid intake practices and possibly different pelvic floor anatomy, requiring further investigation in comparative studies.[13] This regional consistency directly supports the rationale for the present study, confirming that a Pakistan-specific nomogram, rather than an adapted Western or generalized South Asian reference, is required to accurately capture the flow characteristics of the local population and to underpin the age-specific percentile values developed here.

The statistically significant negative correlation between age and Qmax found in our sample group ($r=-0.31$, $p<0.001$), despite the relatively young age group of subjects, is consistent with the physiology of gradual subclinical loss of detrusor muscle contractility starting from the third decade of life. This is shown by the independent association of age as predictor of poor detrusor contractility in absence of bladder obstruction shown by Chen et al.[14] Furthermore, Sinha et al.'s retrospective review database of clinical urodynamic assessment of lower urinary tract dysfunction showed that Qmax starts to decline from age 30 onwards.[15] It can thus be said that the reduction of 4.7 ml/s in the median Qmax from 20–24 to 35–40 years of age in just 20 years is both statistically strong, physiologically feasible, and clinically relevant, as it shows that physiological weakening of voiding capability starts much earlier in Pakistani men than symptoms of BPH or detrusor underactivity appear and seek medical attention. This finding directly informs the age-stratified structure of the nomogram, confirming that a single, non-stratified reference range would misrepresent flow expectations across the studied age bands

As mentioned earlier, the association between voided volume and Qmax ($\beta=0.042$, $p<0.001$) is due to their volume-flow relationship. The voided volume influences flow rate, and thus there should be standardisation in measuring it. Voided volume less than 150 mL has high variance and is generally excluded from analyses, as recommended by the International Continence Society guidelines, in accordance with this research's methodology.[16] Similarly, Kumar et al. found a positive correlation between voided volume and Qmax in India, further demonstrating that these two parameters are related and must be taken into consideration in uroflowmetry studies.[17] This relationship was accordingly incorporated into the percentile tables developed in this study, ensuring that reference values are only applied to voided volumes within the recommended range.

The 12-18% systematic underestimation of normal Qmax with the Liverpool nomogram has clear clinical implications for the management of male patients in Pakistan. It has been proposed that nomograms developed based on non-representative populations may result in biased diagnoses and that the latter cannot be fully controlled for via clinical judgment, hence the need for population-specific norms.[18] However, there are other factors that affect uroflowmetry results, such as voided volume, effort, and symptomatology, and the use of rigid Qmax cutoffs is advised against, according to international guidelines. In this study, Qmax above 16.5 ml/s would be normal by the Liverpool nomogram (>15 ml/s); however, it is actually below the 5th percentile in this cohort (16.8 ml/s). Thus, the inappropriate

application of Western Qmax standards could lead to false normalisations of low values of this parameter.

BMI showed a statistically significant (p=0.046) but weak (r=−0.14) correlation with Qmax in the current study, in line with growing data indicating that higher BMI is associated with reduced Qmax through its impact on urinary flow by causing greater periprostatic fat infiltration, increased intra-abdominal pressure, and altered activity of detrusor smooth muscles.[19] Though BMI was not an independent predictor in the logistic regression analysis of our cohort after accounting for the effects of age and voided volume, further investigations on this topic should be conducted with larger Pakistani samples featuring a wider range of BMIs, taking into consideration the increasing problem of overweight and obesity among Pakistani urban males. As BMI did not independently predict Qmax in this cohort, it was not incorporated as a stratifying variable in the final nomogram, consistent with the study's primary objective of age-based reference values.

Internal validity of the constructed nomograms is evidenced by the split-sample validation ratio of 70:30, resulting in an R^2 value of 0.74 for predicting the Qmax value in the validation sample with no bias on residual analysis. Anderson et al., in their review article, outlined the methodology of nomogram development and internal validation in the field of urology and indicated that the split-sample validation test is the minimum standard for establishing reference intervals for single-center studies, and R^2 values exceeding 0.70 for the validation sample imply sufficient model stability for practical use, criteria met by the current nomograms.[20] Consensus guidelines of the International Continence Society regarding standardization of urodynamics also stressed that a locally devised nomogram must be supplemented with percentile tables to enable the physician to derive reference values without resorting to graph-based calculations exclusively a requirement satisfied by the tables included in this study.

The major strengths of this study include the development of the first age-specific uroflowmetry nomograms for healthy Pakistani men using standardized International Continence Society-recommended uroflowmetry methodology. Strict inclusion and exclusion criteria minimized confounding from lower urinary tract pathology, all uroflowmetry measurements were performed using a calibrated electronic uroflowmeter, and internally validated percentile curves were generated using split-sample validation, improving the reliability of the proposed reference values.

Limitations of this study consist of the single-center nature of participant enrollment conducted in a tertiary care hospital located in the capital city of Islamabad, possibly failing to adequately cover the ethnic, nutritional, and socioeconomic variability of Pakistanis in general, and particularly in other cities and rural areas outside the country's capital, and also comprising only male individuals between the ages of 20 and 40, leaving gaps in developing reference intervals for the 41-70 age group where patients suffer from BPH, detrusor underactivity, and LUTS. Multi-center and nationally representative future research covering the entire adult age range, stratified by province, ethnicity, BMI categories, and fluid intake behavior, are highly recommended to achieve a complete national reference database of uroflowmetry in Pakistan. Furthermore, findings from a relatively modest sample size warrant cautious interpretation, and future studies with larger, multicentre cohorts are recommended to validate these reference values.

Conclusion

Through this research, age-specific uroflowmetric nomograms along with their percentile reference values for Qmax, Qave, voided volume, and voiding time have been formulated for healthy young adult Pakistani males. The reference values obtained through this research will act as the standard population-specific reference for interpreting uroflowmetric results of Pakistani males keeping in view the limitations of study. The nomograms generated through this study may act as a base for future validations and use in clinical practice.

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