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Original Article

EVALUATION OF FACTORS AFFECTING INTRAOPERATIVE AND POSTOPERATIVE HEMORRHAGE IN PERCUTANEOUS NEPHROLITHOTOMY

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Abstract:

Objective: *There are many factors that are thought to affect hemorrhage associated with Percutaneous Nephrolithotomy (PCNL). This study was designed to evaluate factors affecting intraoperative and postoperative hemorrhage associated with PCNL.*

Patients and Methods: *This prospective observational study was carried out in the Department of Urology, National Institute of Kidney Diseases and Urology, Dhaka, from December 2020 to December 2021. Total 87 patients with renal stone were selected by purposive sampling. Blood loss was estimated by the postoperative drop in hemoglobin and hematocrit after 48 hours of operation. Association of five patient-related factors (Diabetes mellitus, Hypertension, renal parenchymal thickness, stone burden and previous ipsilateral intervention) and five procedure-related factors (size of the tract, number of tracts, operation time, calyx of puncture and intraoperative complications) with hemorrhage was assessed using multiple linear regression analysis. Analysis of means was done by Independent sample t-test and one-way ANOVA test.*

Results: *The mean ± SD for hemoglobin and hematocrit drop was 1.95 ± 0.87 gm/dl and 6.18 ± 2.36 % respectively. Multiple linear regression analysis showed that Diabetes mellitus (P=0.001), Hypertension (P=0.01), Renal parenchymal thickness (P=0.03), Stone burden (P=0.02), Previous ipsilateral intervention (P=0.001), Size of the tract (P=0.0001), Number of tracts (P=0.0001), Operation time (P=0.004) and Intraoperative complications (P=0.0001) were significant predictors of hemorrhage. Overall blood transfusion rate for all patients was 17.24 %. Diabetes mellitus, Number of tracts, Operation time and Intraoperative complications were significant predictor of perioperative blood transfusion requirement. One factor- Calyx of puncture, was found to have no effect on hemorrhage.*

Conclusion: *Diabetes mellitus, Hypertension, increased stone burden, larger tract size, multiple tracts, prolonged operation time and occurrence of intraoperative complications are associated with increased hemorrhage during and after PCNL. Atrophic renal parenchyma and previous ipsilateral intervention are associated with reduced hemorrhage.*

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Percutaneous Nephrolithotomy, Hemorrhage, Factors, Intraoperative, Postoperative

Introduction

Nephrolithiasis is one of the common urological diseases throughout the world because of its high incidence, prevalence and recurrence rate. It is the third most common clinical problem of urinary system, exceeded only by urinary tract infections and pathologic conditions of the prostate.[1] About half of the patients treated previously develop recurrent renal

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stone within 5-7 years. In Bangladesh, renal stone disease is more common in northern part of the country. It is most prevalent between the ages of 20 to 40 years. The highest incidence of stone disease occurs in the summer months, July through September due to seasonal high ambient temperature.[2]

Among different modalities of treatment for renal stone clearance, percutaneous nephrolithotomy (PCNL) is considered gold-standard due to higher stone clearance rates, better cost-effectiveness and early convalescence.[3] PCNL was first successfully performed in 1976, by FernstrÖm and Johansson who extracted renal calculus through a percutaneous nephrostomy under radiological control.[4] Although technological refinements and increased surgical experience have ensured the procedure's successful execution, PCNL is associated with complications like hemorrhage, collecting system injury, adjacent organ injury (pleura, lung, colon, liver, spleen), fluid extravasation & absorption, residual stone, hematuria, urosepsis, renocutaneous fistula, intrarenal pseudoaneurysm, renovascular A-V fistula etc.[5] Of these complications, hemorrhage during and after PCNL is the most common, worrisome and unpredictable complication.[6] In kidney, a high-flow arteriovenous network constituting 20% of the total cardiac output closely surrounds the collecting system. Among these, segmental and interlobar vessels are significant. Access to pelvicaliceal system and intrarenal manipulation may traumatize these vessels, resulting in significant bleeding.[7,8] Although most bleeding can be managed conservatively (bedrest, blood transfusion, antibiotic etc.), intractable bleeding may require renal angiography with selective angioembolization and sometimes nephrectomy to save the life.

It has been suggested that there are some risk factors which influence hemorrhage during and after PCNL. A number of studies had been carried out to evaluate such predictive factors in different countries. In these studies, various patient-related and procedure-related factors have been assessed. But there are controversies among different studies regarding the affecting factors which lead to evaluate these factors again in the context of our population as PCNL is being performed increasingly day by day in our country and surgeons have to face this complication and manage it frequently. So it is necessary to evaluate the role of these factors in hemorrhage during and after PCNL in the context of our population. Determination of such factors will help to detect high risk patients and thereby setting strategy to manage bleeding more efficiently, to arrange intervention (angiography and therapeutic embolization) at appropriate time if necessary, and ultimately to reduce PCNL related morbidity and mortality.

Materials and Methods

This prospective observational study was carried out in the department of Urology, National Institute of Kidney Diseases and Urology (NIKDU), Sher-e-Bangla Nagar, Dhaka, from December 2020 to December 2021. Sampling technique was purposive sampling, so patients with renal stone who fulfill inclusion and exclusion criteria got admitted for PCNL through OPD were enrolled in this study using purposive sampling technique.

Sample size is determined using following formula:

$$\mathbf{n} = \frac{\boldsymbol{\sigma}^2 \times (\boldsymbol{z}_\alpha + \boldsymbol{z}_\beta)^2}{(\boldsymbol{\mu} - \boldsymbol{\mu}_0)^2}$$

Here,

n = sample size

σ = population Standard Deviation (SD)

From previous study it is 1.23 [3]

$Z\alpha$ = z-value of Standard Normal Distribution (SND) at a given level of significance/confidence

For this study, 5% level of significance (95% confidence level) is determined.

So, at 5% level of significance or 95% confidence level z-value is 1.96

=1.96

$Z\beta$ = z-value of Standard Normal Distribution (SND) at a given power.

At 80% power it is 0.85

= 0.85

μ = anticipated value/ population mean which is proposed to be found

= 2.11

μ_0= standard value/ population mean from previous study [3]

= 1.68

So, $$\mathrm{n} = \frac{(1.23)^2 \times (1.96 + 0.85)^2}{(2.11 - 1.68)^2}$$

$$= 64.6$$

Our initial proposed sample size was 65. Because of availability of cases, 87 patients were included in this study.

Patients who had renal stone of greater than 2 cm size, aged older than 18 years and below 70 years, upper ureteric stone, recurrent renal stone with H/O previous ipsilateral intervention (open surgery, PCNL, ESWL) were included in this study. Patients who had untreated UTI, uncorrected bleeding disorder, on

antiplatelet or anticoagulant drugs, Preexisting anemia (Hb% < 10gm/dl), stone in solitary or ectopic or transplanted or non-functioning kidney, stone with congenital renal anomalies like horseshoe or malrotated kidney, morbid obesity and medical renal disease were excluded from this study.

Ethical clearance for the study was taken from the Ethical Review Committee, National Institute of Kidney Diseases & Urology. Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, the patients and their guardians were informed verbally about the study design, purpose of the study and their right to withdraw themselves from the study at any time, for any reason, whatsoever. An informed written consent form was provided to all patients. Only the patients who gave written consent were included as study sample.

In this study ten factors were analyzed. Five were patient-related and another five were procedure-related. Patient-related factors were Diabetes mellitus, Hypertension, renal parenchymal thickness, stone burden and previous ipsilateral intervention (open stone surgery, PCNL, ESWL). Procedure-related factors were size of the tract, number of tracts, operation time, calyx of puncture and intraoperative complications. To achieve our goal we measured post-operative (48 hours later) Hemoglobin and Hematocrit drop and observed which patients needed blood transfusion due to intraoperative and post-operative blood loss.

CBC of all patients was done before and 48 hours after PCNL. Number of unit of whole blood transfused between the preoperative period and the final CBC was recorded if needed. The approximation that 1 unit of blood transfusion increases the hemoglobin level by 1.0 gm/dl and the hematocrit by 3% was used to factor the influence of blood transfusion in estimation of hemorrhage. The total hemorrhage in respect to Hb drop was calculated using the following formula:

[(preoperative Hb - postoperative Hb) + (number of blood unit transfused x 1)][3]

The total hemorrhage in respect to Hct drop was calculated using the following formula:

[(preoperative Hct - postoperative Hct) + (number of blood unit transfused x 3)][3]

All patients were divided in subgroups for each predetermined factors which has been shown in Table 1. Renal parenchymal thickness was measured preoperatively from non-contrast film of CT scan of KUB. Stone burden was calculated from plain X-ray KUB 100% film for radiopaque stone and non-contrast CT scan of KUB. The association of total blood loss and transfusion requirement with various factors was evaluated by standard multiple regression analysis using the SPSS software, version 25. Mean and Standard Deviation were used for description of quantitative data and Frequencies for categorical data. Comparison of mean was done by Independent sample t-test and One-way ANOVA test. 95% confidence interval was used. P value of less than 0.05 was considered significant.

Results:

Data were found from all the 87 patients and there was no dropout of patients because all data were collected during the period of hospital admission before discharge. Frequency distribution of different subgroup for each factors is shown in Table I. Multiple regression of different patient and procedure related factors in respect to Hb drop, Hct drop and BT requirement are shown in Table II, III, IV. Effect of individual factor on blood loss shown in Table V. Assumptions of linear regression (normality, multicollinearity, homoscedasticity) were tested. The adjusted R square value for Hemoglobin drop as outcome variable was 0.838, for Hematocrit drop 0.841 and for Blood Transfusion 0.812.

Table-I

Frequency % of analyzed factors (N=87)

Factors	Subcategorization	Frequency (%)
Diabetes Mellitus	Yes	35 (40.23 %)
	No	52 (59.77 %)
Hypertension	Yes	36 (41.38 %)
	No	51 (58.62 %)
Renal parenchymal	<10 *mm*	17 (19.54 %)
thickness	>10 *mm*	70 (80.46 %)
Stone burden	<500 mm^2	25 (28.74 %)
	500-1000 mm^2	49 (56.32 %)
	>1000mm^2	13 (14.94 %)
Previous ipsilateral intervention	Yes	12 (13.79 %)
	No	75 (86.21 %)
Size of the tract	<20 Fr	52 (59.77 %)
	20-24 Fr	23 (26.44 %)
	26-30 Fr	12 (13.79 %)
Number of tracts	1	69 (79.31 %)
	2	18 (20.69 %)
Calyx of puncture	Lower	35 (40.23 %)
	Middle	27 (31.03 %)
	Upper	7 (8.05 %)
	Lower and middle	18 (20.69 %)
Operation time	<60 min	13 (14.94 %)
	60-90 min	53 (60.92 %)
	>90 min	21 (24.14 %)
Intraoperative	Present	22 (25.29 %)
complications	Absent	65 (74.71 %)

Table-II

Multiple regression of analyzed factors with Hb drop as dependent variable

Factors	Standardized Coefficients Beta	95% Confidence Interval Lower Bound	Upper Bound	P value
Diabetes Mellitus	0.174	0.132	0.482	0.001
Hypertension	0.017	0.145	0.171	0.01
Renal parenchymal thickness	0.117	0.029	0.485	0.03
Stone burden	0.173	0.032	0.433	0.02
Previous ipsilateral intervention	-0.189	-0.757	-0.196	0.001
Size of the tract	0.278	0.193	0.457	0.0001
Number of tracts	0.466	0.542	1.457	0.0001
Calyx of puncture	-0.111	-0.224	0.056	0.24
Operation time	0.203	0.093	0.477	0.004
Intraoperative complications	0.232	0.269	0.660	0.0001

Data analysis was done by Standard multiple regression test. P value < 0.05 was considered significant. Hb= Hemoglobin.

Table-III

Multiple regression of analyzed factors with Hct drop as dependent variable

Factors	Standardized Coefficients Beta	95% Confidence Interval Lower Bound	Upper Bound	P value
Diabetes Mellitus	0.178	0.381	1.315	0.001
Hypertension	0.013	0.405	0.438	0.02
Renal parenchymal thickness	0.125	0.130	1.346	0.02
Stone burden	0.201	0.193	1.264	0.01
Previous ipsilateral intervention	-0.202	-2.119	-0.621	0.0001
Size of the tract	0.287	0.553	1.304	0.0001
Number of tracts	0.460	1.437	3.882	0.0001
Calyx of puncture	-0.133	-0.647	0.102	0.15
Operation time	0.185	0.189	1.214	0.01
Intraoperative complications	0.210	0.609	1.655	0.0001

Data analysis was done by Standard multiple regression test. P value < 0.05 was considered significant. Hct= Hematocrit.

Table-IV

Multiple regression of analyzed factors with BT requirement as dependent variable

Factors	Standardized Coefficients Beta	95% Confidence Interval Lower Bound	Upper Bound	P value
Diabetes Mellitus	0.231	0.047	0.308	0.008
Hypertension	-0.005	-0.121	0.114	0.95
Renal parenchymal thickness	-0.025	-0.194	0.146	0.78
Stone burden	-0.022	-0.162	0.137	0.87
Previous ipsilateral intervention	0.033	-0.173	-0.246	0.73
Size of the tract	0.088	-0.059	0.151	0.39
Number of tracts	0.410	0.041	0.724	0.03
Calyx of puncture	-0.028	-0.114	0.095	0.86
Operation time	0.266	0.019	0.305	0.03
Intraoperative complications	0.446	0.241	0.533	0.0001

Data analysis was done by Standard multiple regression test. P value < 0.05 was considered significant. BT= Blood Transfusion.

Table-V

Effect of individual factor on blood loss in respect to Hb & Hct drop

Predetermined factors	Hb drop (gm/dl)		Hct drop (%)	
	Mean ± SD	P value	Mean ± SD	P value
Diabetes mellitus				
Yes (n=35)	2.19 ± 0.80	0.04	6.89 ± 2.13	0.02
No (n=52)	1.79 ± 0.89		5.75 ± 2.39	
Hypertension				
Yes (n=36)	2.05 ± 0.83	0.003	6.47 ± 2.22	0.002
No (n=51)	1.87 ± 0.90		5.99 ± 2.45	
Renal parenchymal thickness				
< 10 mm (n=17)	1.24 ± 0.53	<0.0001	4.25 ± 1.56	<0.0001
>10 mm (n=70)	2.12 ± 0.86		6.65 ± 2.28	
Previous ipsilateral intervention				
Yes (n=12)	1.10 ± 0.17	<0.0001	3.83 ± 0.50	<0.0001
No (n=75)	2.08 ± 0.87		6.56 ± 2.32	
Number of tracts				
01 (n=69)	1.69 ± 0.76	<0.0001	5.50 ± 2.12	<0.0001
02 (n=18)	2.94 ± 0.46		8.79 ± 1.05	
Intraoperative complications				
Present (n=22)	2.58 ± 0.77	<0.0001	7.82 ± 1.90	<0.0001
Absent (n=65)	1.73 ± 0.81		5.63 ± 2.25	
Stone burden				
<500 mm^2 (n=25)	1.02 ± 0.16		3.58 ± 0.50	
500 – 1000 mm^2 (n=49)	2.10 ± 0.67	<0.0001	6.68 ± 1.79	<0.0001
>1000 mm^2 (n=13)	3.15 ± 0.39		9.35 ± 0.73	
Size of the tract				
<20 Fr (n=52)	1.68 ± 0.86		5.43 ± 2.32	
20 – 24 Fr (n=23)	2.20 ± 0.72	0.001	6.94 ± 1.89	0.001
26 – 30 Fr (n=12)	2.60 ± 0.75		8.03 ± 1.91	
Operation time				
<60 min (n=13)	1.12 ± 0.24		3.93 ± 0.72	
60 – 90 min (n=53)	1.80 ± 0.71	<0.0001	5.83 ± 2.01	<0.0001
>90 min (n=21)	2.83 ± 0.79		8.46 ± 1.99	
Calyx of puncture				
Lower (n=35)	1.88 ± 0.78		6.07 ± 2.16	
Middle (n=27)	1.40 ± 0.68	0.061	4.67 ± 1.85	0.073
Upper (n=7)	1.72 ± 0.70		5.63 ± 2.05	
Lower & middle (n=18)	2.94 ± 0.46		8.79 ± 1.05	

Comparison of mean was done by Independent sample t-test for Diabetes mellitus, Hypertension, Renal parenchymal thickness, Previous ipsilateral intervention, Number of tracts and Intraoperative complications. One-way ANOVA test was used for comparison of mean in case of stone burden, Size of the tract, Operation time and Calyx of puncture. P value <0.05 was considered significant. Hb= Hemoglobin, Hct=Hematocrit, gm=gram, dl=deciliter.

Discussion

This study has been designed to evaluate the effect of some patient and procedure related factors on intraoperative and postoperative hemorrhage in PCNL. There are many suspected predictive factors but in this study factors that are most practical and frequently encountered in our practice had been analyzed whether they had positive, negative or no effect. All the factors were evaluated on the basis of three outcome variables- Hemoglobin drop, Hematocrit drop and Blood Transfusion requirement. Postoperative hemoglobin level might not be at equilibrium, depending on the hemostatic and hydration status of the patient. Use of hemoglobin level at least 48 hours after PCNL was an attempt to minimize hydration artifacts from intravenous fluid administration and absorption of retroperitoneal fluid. Concurrent estimation of hematocrit decrease was done to correct the effect of hemodilution.

Standard multiple regression analysis revealed that, among the factors Diabetes Mellitus, Hypertension, Renal parenchymal thickness, Stone burden, Previous ipsilateral intervention, Size of the tract, Number of tracts, Operation time and Intraoperative complications demonstrated significant association with blood loss or hemorrhage. Among these, Size of the tract, Number of tracts and Intraoperative complications were the most significant predicting factors. Whereas Calyx of puncture showed no association with hemorrhage.

Overall Blood transfusion rate for all patients was 17.24 % (15 patients). All patients who required blood transfusion received 01 unit of fresh whole blood. Standard multiple regression analysis with blood transfusion requirement as the outcome variable revealed that, Diabetes Mellitus, Number of tracts, Operation time and Intraoperative complications were predictive factors of blood transfusion requirement.

Among 87 patients, 40.23% patients were diabetic. Diabetic patients had more blood loss than non-diabetic ones which was proved by statistically significant difference in both mean Hb drop and mean Hct drop. In other study they also found that Diabetes mellitus increases intraoperative and postoperative hemorrhage.[3,9,10] In diabetic patients, associated arteriosclerosis with thickened basement membrane causes increased bleeding after the initial trauma of tract formation.

In this study, <10mm renal parenchymal thickness was considered as atrophic parenchyma. Total 19.54% patients had atrophic parenchyma. Patients with atrophic renal parenchyma experience less blood loss than with normal parenchyma. This finding was consistent with the results observed in other study.[3,11,12] But other found that increased degree of HDN, that means thinning of renal parenchyma was associated with more blood loss.[13] While other showed that renal parenchymal thickness at puncture site did not predict peroperative hemorrhage in PCNL.[14] Reduced hemorrhage in atrophic renal parenchyma may be due to atrophy of intrarenal vasculature.

Effect of stone burden on hemorrhage was significant. The larger stone, the more blood loss occurred. This was comparable with the results observed in other studies.[10,15,16] While other found that stone surface area did not correlate with bleeding.[3] Actually increased stone surface area necessitates increased tract size, multiple tracts, prolonged operation time and also increases the occurrence of intraoperative complications, thus results in greater blood loss.

Previous ipsilateral intervention included any one of ESWL, open surgery or PCNL in this study. Comparison of blood loss between patients having previous ipsilateral intervention (13.79%) or not (86.21%) showed significant decrease of blood loss in former group. Finding was similar to other study.[3] But others mentioned in their study that previous intervention was associated with increased blood loss.[17,18] Their explanation was that distorted anatomy due to previous surgery was associated with more intraoperative manipulation & bleeding. While other found that previous ipsilateral open renal stone surgery had no effect on bleeding.[19] In our perspective, previous intervention is associated with fibrosis of renal tissue which is relatively less vascular and reduces bleeding.

For this study, Nephroscopes of three calibers were used – 12 Fr, 18 Fr (with 22 Fr sheath), and 24 Fr. Access tracts were dilated accordingly. It was found that, bleeding increased when tract caliber was increased. Similar findings had been mentioned by other in their study.[12] Increased tract size associated with more vascular and renal tissue injury thus increased hemorrhage.

Total 18 patients underwent double puncture in this study for stone complexity and increased stone size.

Analysis of number of tracts showed that double tracts were associated with more hemorrhage than with single tract. It was consistent with the results observed in other study.[3,9,10,17,20,21]

Total operation time were subdivided into 3 categories - <60 min (14.94 % patients), 60-90 min (60.92 % patients) and >90 min (24.14 % patients). It was found that, bleeding increased when the operation time increased. In other study they also found that prolonged operation time was associated with significantly increased hemorrhage.[9,11,12,13] Prolonged operation time is commonly associated with intraoperative complications, larger stone, more intrarenal manipulation, all of which increase blood loss.

For this study intraoperative complications were consisted of – infundibular tear and renal pelvic perforation. Among 87 PCNL surgeries, intraoperative complications occurred in 22 cases. Statistical analysis showed that occurrence of intraoperative complications was significantly associated with increased hemorrhage in PCNL. Other mentioned similar finding in their studies.[8,17.18]

In this study, 41.38% patients were hypertensive and rest of the patients were normotensive (58.62%). Hypertensive patients had more blood loss than normotensive ones which was proved by statistically significant difference in both mean Hb drop and mean Hct drop. Although other mentioned that HTN did not have any effect on blood loss[3], we found HTN as significant predictor of hemorrhage in PCNL.

Among ten predictive factors, only calyx of puncture was found not to affect hemorrhage during and after PCNL significantly. Few studies found that middle calyceal access was associated with significant blood loss[20,22] but no significant association between middle calyceal puncture and increased hemorrhage was found in this study.

Conclusion

From the result of this study it may be concluded that, diabetes mellitus, hypertension, renal parenchymal thickness, stone burden, previous ipsilateral intervention, size of the tract, number of tracts, operation time and intraoperative complications significantly affect intraoperative and postoperative hemorrhage in PCNL. Among these, diabetes mellitus, hypertension, increased stone burden, larger access tract size, multiple access tracts, prolonged operation time and occurrence of intraoperative complications are associated with more hemorrhage. Whereas atrophic renal parenchyma (due to HDN by Stone) and previous ipsilateral intervention (ESWL, PCNL, or open Surgery) are associated with less hemorrhage. Calyx of puncture has no significant effect on hemorrhage in PCNL. Diabetes mellitus, multiple tracts, prolonged operation time and occurrence of intraoperative complications are associated with requirement of blood transfusion.

Recommendations

From this study, measures that may reduce hemorrhage and blood transfusion rate associated with PCNL are- access tract caliber and number should be kept as minimum as possible without compromising stone clearance; operation time should not be prolonged, when it is going to be prolonged procedure should be staged and intraoperative complications should be tried to avoid or decrease. Blood transfusion may be required when patient is diabetic, multiple tracts have been made, operation time becomes prolonged and intraoperative complications have been occurred. Further prospective large scale multicenter study is suggested to verify the present study results.

Limitations of the study

This study had several limitations- purposive sampling, small sample size, factors were predetermined, delayed post-PCNL bleeding was not included and limited number of factors were included.

Conflict of interest: None to disclose

Ethical approval: Approved from IRB, National Institute of Kidney Diseases and Urology (NIKDU), Sher-e-Bangla Nagar, Dhaka.

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