



Original Research Article

Histopathological study of crossing vessels an associated finding or cause in pelviureteric junction obstruction

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ABSTRACT

Introduction and Objectives: Most common cause for pelviureteric junction (PUJ) obstruction is thought to be intrinsic defect of muscular development or the deficient nerves in the obstructed narrow segment. Other causes include obstruction from outside: crossing vessel (CV), tumor compressing PUJ etc and intramural causes. Congenital Hydronephrosis is associated with crossing vessels in 26% of cases. The purpose of this work is to evaluate histopathological changes in patients of PUJ obstruction with or without crossing vessels.

Materials and Methods: This was a prospective study conducted on 128 patients who underwent pyeloplasty from January 2016 to June 2018. Of these 42 patients had associated crossing vessels. Histopathological analysis of PUJ segment was done to look for chronic inflammation, muscular hypertrophy, fibrosis, muscle disarray and synaptophysin.

Results: Moderate to severe chronic inflammation was seen in 23.8% and 44.2% ($P > 0.05$) cases with CV and without CV respectively, similarly fibrosis and muscular hypertrophy was seen higher in cases without CV although these were not statistical significant. On contrary muscle disarray shows trend of higher in cases with CV but it was also not statistical significant. Synaptophysin was positive in 4.8% cases with CV and 4.7% cases without CV.

Conclusion: Based on this study there is no significant statistical difference in the histopathological changes in patients with or without crossing vessels. So crossing vessel is not the cause but an associated finding in pelvi-ureteric junction obstruction.

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1. Introduction

Intrinsic defect of muscular development or due to deficient nerves in the obstructed narrow segment of PUJ is thought to be most common cause for PUJ obstruction. Other causes include obstruction from extrinsic compression (crossing vessel, tumor compressing PUJ, fibrous cord, enlarged lymph node compressing the PUJ etc., Intramural pathology (fibrosis of PUJ due to previous surgery or stones, or tumor of the wall of PUJ.) Intraluminal pathology (stones, polyp, mucosal folds etc.) 26% of cases present with congenital hydronephrosis are associated with crossing or aberrant vessels. Sampaio et al study found that 65%

relation to the anterior surface of the PUJ of crossing vessels and 45% of these cases the relationship with the inferior segmental artery.¹ Van Canghai et al found an associated vessel in 39% of patients with PUJ obstruction on digital angiography.²

Crossing vessel is a misnomer and it is actually a lower polar segmental artery appropriate called as “vascular bar”³ it is end artery. It is not the primary cause of PUJ obstruction rather PUJ is already obstructed due to intrinsic defect and it only causes partial obstruction and leading redundant pelvis kinks and falls upon the vessel increasing hydronephrosis.⁴ Others authors hypothesized that this vessel is the mere cause of obstruction and its transposition required in the management.⁵ The purpose of

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this work is to evaluate histopathological changes in PUJO with or without crossing vessels and to find out whether this is the cause of obstruction or PUJ is congenitally obstructed by intrinsic muscular defect or nerve deficiency.

2. Aim and Objective

1. To compare histopathological changes between crossing vessels PUJO and without crossing vessels PUJO.
2. To identify whether crossing vessel is the only cause for PUJO without any intrinsic defect or it is the associated finding in PUJO with intrinsic defect.

3. Material and Methods

Study Setting: This study is carried out at Ram Manohar Lohia, tertiary care hospital in Department of Pathology, Lucknow from January 2016 to June 2018.

Study Type: The present study was prospective of 128 patients who follow the inclusion and exclusion criteria underw ent pyeloplasty surgery.

Study Group: Out of 128 patients participated in the study 42 patients had associated crossing vessels and 86 patients not associated with crossing vessels.

The ratio of patients with PUJ obstruction with crossing vessels versus without crossing vessels was 1:2.

3.1. Inclusion criteria

The patients with the following characteristics were included in the study.

1. All the patients who underwent pyeloplasty
2. Patients giving consent to enter the study

3.2. Exclusion criteria

1. Patients who underwent redo pyeloplasty.
2. Patients not giving consent to enter the study

3.3. Assesment

Institutional Ethical Committee approval was obtained. Patients giving informed consent from patients fulfilling the inclusion criteria were included. The number of cases of crossing vessels and their histopathological findings and presence or absence of synaptophysin was recorded on a specially designed proforma.

3.4. Histological assesment

Histologically we assessed for inflammation, fibrosis, muscle hypertrophy, pattern smooth muscle and synaptophysin.

All PUJ segments had previously undergone fixation in 10% (wt/vol) phosphate-buffered in formalin for 24-48 hours. After doing standard histological processing and embedding in paraffin, 5 micromilimeter thick sections

were used for H&E staining that was used for diagnostic pathology like inflammation, fibrosis, muscle hypertrophy and muscle disarray and immunohisto chemistry done to look for synaptophysin. The H&E slides were reviewed by senior pathologist, blinded to the etiology. Urothelium was evaluated for presence or absence of metaplasia/ dysplasia. In lamina propria layer, presence of fibrosis (0 = none; mild = limited to lamina propria ; moderate = involving muscularis propria ; severe= replacing muscularis propria and extending into adventitial layer) and inflammation (divided into mild, moderate and severe) evaluated. Special stain for Masson's Trichrome used when necessary to differentiate between fibrosis from smooth muscle hyperplasia and define muscle disarray. Synaptophysin staining was done to look for Ganglion cells in the wall.

3.5. Statistical analysis

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0 Continuous variables are presented as mean±SD, and categorical variables are presented as absolute numbers and percentage.

The comparison of normally distributed continuous variables between the groups was performed using students t pair test. Nominal categorical data between the groups were compared using chi square test or Fischers exact test as appropriate. P<0.05 was considered statistically significant.

4. Ethical issues

The study does not effect on the primary treatment protocol. There were no adverse changes due to study results, and also permit the early diagnosis of complications. Blood collection for analysis has been added to the routine blood sampling. There was minimal escalation of treatment costs owing to increased number of investigations, details of which was explained in the informed consent.

5. Observations & Results

As per inclusion criteria and other parameters of this study, 128 patients were part of this study with pelviureteric junction (PUJ) obstruction at Department of pathology, RML Lucknow, from January 2016 to June 2018.

Table 1: Group distribution

Groups	Frequency	%
Crossing vessel	42	32.8%
Non crossing vessel	86	67.2%
Total	128	100%

The distribution of the patients according to the two groups i.e. Crossing Vessel and Non Crossing Vessel. It was observed that 67.2% of the patients were in Non crossing

vessel while 32.8% patients were in Crossing Vessel Group. (Table 1)

Table 2: Comparison of Mean Age between Crossing vessel and Non crossing vessel

	Crossing vessel (n=21)	Non crossing vessel (n=43)	P Value
	Mean ± SD	Mean ± SD	
Age	29.57 ± 10.50	30.05 ± 9.94	0.861

The mean age between the two groups under the study was observed that the mean age of Crossing Vessel group was 29.57 ± 10.50 years while for Non Crossing vessel group the mean age was 30.05 ± 9.94 years. Further it was observed that there was no significant difference in mean age of the two groups (p value of 0.861). (Table 2)

The comparison of age distribution of the patients between the two groups under the study. It was observed that under the group Crossing level, 33.3% of the patients were in age group 2, 28.6% were in age group 3, 23.8% were in age group 1 and 14.3% of the patients were in age group 4. Similarly for the group Non crossing vessel, 46.5% of the patients were in age group 2, 18.6% of the patients each were in age groups 3 & 4 and 16.3% patients were in age group 1. further, it was observed that there was no significant difference in age distribution when compared between the two groups (P value of 0.615). (Table 3)

The comparison of gender distribution of the patients between the two groups under the study. It was observed that under the group Crossing level, 71.4% of the patients were males while 28.6% were females. Under the group Non crossing vessel, 62.8% of the patients were males while 37.2% were females.

Further, it was observed that there was no significant difference in gender distribution when compared between the two groups (P value of 0.495). (Table 4)

The comparison of distribution of the patients according to Diagnostics between the two groups under the study. It was observed that under the group Crossing vessel, 66.7% of the patients were diagnosed with Right sided PUJO while 33.3% were diagnosed with Left sided PUJO. Under the group Non Crossing vessel, 53.5% of the patients were diagnosed with Right sided PUJO while 46.5% were diagnosed with Left sided PUJO.

Further, it was observed that there was no significant difference in between the two groups (P value of 0.316).(Table 5)

The comparison of distribution of the patients according to Mild and Moderate to severe inflammation between the two groups under the study. It was observed that under the group Crossing vessel, 76.2% of the patients shows Mild inflammation while 23.8% shows Moderate to severe inflammation. Under the group Non Crossing vessel, 55.8% of the patients shows Mild inflammation while 44.2% shows Moderate to severe inflammation.

Further, it was observed that there was no significant difference between the two groups (p value of 0.114). (Table 6)

The comparison of distribution of the patients according to Fibrosis between the two groups under the study. It was observed that under the group Crossing Vessel, 28.6% of the patients shows Mild fibrosis while 71.4% shows moderate to severe fibrosis. Under the group Non Crossing Vessel, 23.3% of the patients shows Mild fibrosis while 76.7% shows Moderate to severe fibrosis. Further, it was observed that there was no significant difference between the two groups (p value of 0.645).(Table 7)

The comparison of distribution of the patients according to synaptophysin between the two groups under the study. It was observed that 1 patient (4.8%) in Crossing Vessel group and 2 patients (4.7%) Non Crossing group were positive for synaptophysin.

Further, it was observed that there was no significant difference *between the two groups*.(Table 8)

The comparison of distribution of the patients according to MH between the two groups under the study. It was observed that under the group Crossing Vessel, 52.4% of the patients were under Mild MH while 47.6% were under Moderate to severe MH. Under the group Non Crossing Vessel, 69.8% of the patients were under Mild MH while 30.2% were under Moderate to severe MH. Further, it was observed that there was no significant difference between the two groups (p value of 0.173). (Table 9)

The table and chart above shows the comparison of distribution of the patients according to Muscle Diarray between the two groups under the study. It was observed that under the groups Crossing Vessel 28.6% of the patients had Muscle Diarray. And under Non Crossing Level, 7% of the patients had Muscle Diarray.

Further, it was observed that there was a significant difference between the two groups (p value of 0.049). (Table 10)

The histopathological analysis between these 2 groups shows no statistical significant (Table 11).

6. Discussion

Exact pathophysiology of UPJ obstruction remains controversial. Derangement of the muscle arrangement, atrophy /decrease of myocytes, decrease in interstitial cells of Cajal, reduction of nerve terminals and increased collagen deposition between muscle bundles would explain the decrease of distensibility at the obstructed segments, and may contribute to the absence of the ureteropelvic muscular contractions.⁶⁻⁹ On the other hand, some investigators believe that intrinsic defect of muscle cells is the mechanism of obstruction and the morphological features may arise as the secondary changes.¹⁰

Significant crossing vessels have been noted in up to 63% of patients with UPJO but in as little as 20% of individuals

Table 3: Comparison of age group distribution between crossing vessel and Non crossing vessel

Age Groups	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
13 - 20yrs	10	23.8%	14	16.3%	0.615
21 - 30yrs	14	33.3%	40	46.5%	
31 - 40yrs	12	28.6%	16	18.6%	
41 - 50yrs	6	14.3%	16	18.6%	
Total	42	100%	86	100%	

Table 4: Comparison of Sex distribution between Crossing vessel and Non crossing vessel

Sex	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
F	12	28.6%	32	37.2%	0.495
M	30	71.4%	54	62.8%	
Total	42	100%	86	100%	

Table 5: Comparison of Diagnosis between Crossing vessel and Non crossing vessel

Diagnosis	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
L PUJO	14	33.3%	40	46.5%	0.316
R PUJO	28	66.7%	46	53.5%	
Total	42	100%	86	100%	

Table 6: Comparison of inflammation in PUJ segment between Crossing vessel and Non crossing vessel

M/M-S	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
M	32	76.2%	48	55.8%	0.114
M-S	10	23.8%	38	44.2%	
Total	42	100%	86	100%	

Table 7: Comparison of fibrosis in PUJ segment between Crossing vessel and Non crossing vessel

F	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
M	12	28.6%	20	23.3%	0.645
M-S	30	71.4%	66	76.7%	
Total	42	100%	86	100%	

Table 8: Comparison of synaptophysin in PUJ segment between Crossing vessel and Non crossing vessel

N	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
Positive	2	4.8%	4	4.7%	1.000
Negative	40	95.2%	82	95.3%	
Total	42	100%	86	100%	

Table 9: Comparison of Muscle Hypertrophy(MH) in PUJ segment between Crossing vessel and Non crossing vessel

MH	Crossing vessel		Non crossing vessel		P Value
	Frequency	%	Frequency	%	
M	22	52.4%	60	69.8%	0.173
M-S	20	47.6%	26	30.2%	
Total	42	100%	86	100%	

Table 10: Comparison of Muscle Diarray between Crossing vessel and Non crossing vessel

	Crossing vessel (n=21)		Non crossing vessel (n=43)		P Value
	Frequency	%	Frequency	%	
Muscle Diarray	10	23.8%	6	7.0%	0.102

Table 11: Histopathological analysis of crossing vessels and noncrossing vessels group

		Crossing vessel		Non crossing vessel		P Value
		Frequency	%	Frequency	%	
I	M	16	76.2%	24	55.8%	0.114
	M-S	5	23.8%	19	44.2%	
F	M	6	28.6%	10	23.3%	0.645
	M-S	15	71.4%	33	76.7%	
N	Positive	1	4.8%	2	4.7%	1.000
	Negative	20	95.2%	41	95.3%	
MH	M	11	52.4%	30	69.8%	0.173
	M-S	10	47.6%	13	30.2%	
Muscle Diarray		5	23.8%	3	7.0%	0.102

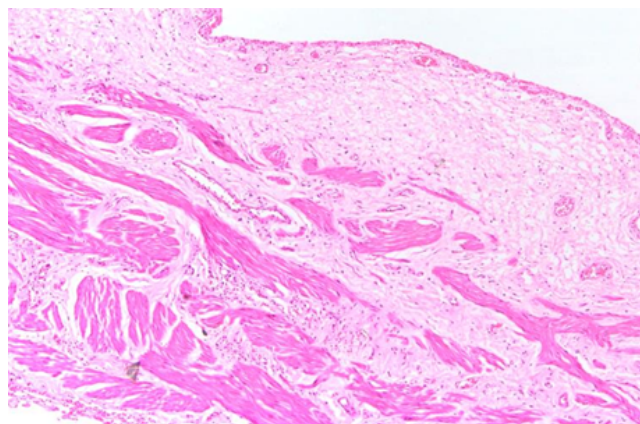


Fig. 1: H & E View of Puj Segment

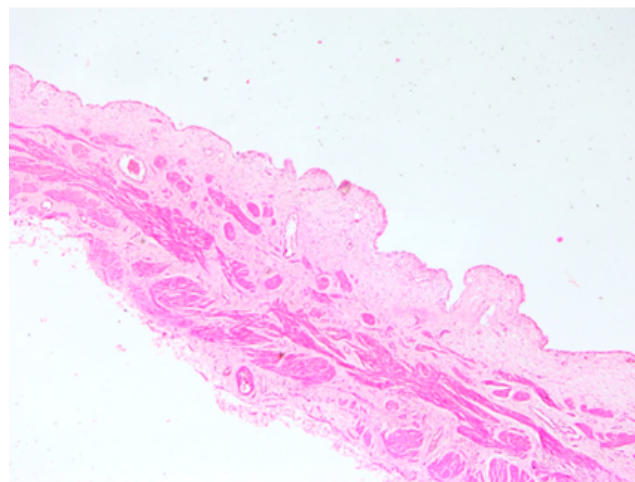


Fig. 3: 5x HE fibrosis gr1, mild muscle hypertrophy, absent muscle disarray of puj segment

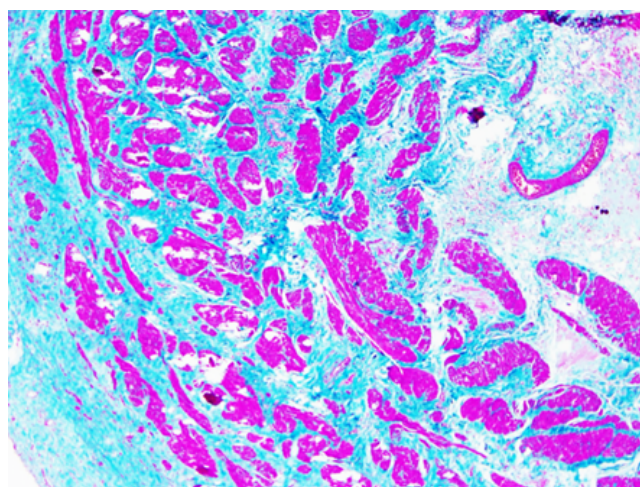


Fig. 2: H & E MT Fibrosis Grade 2 of Puj Segment

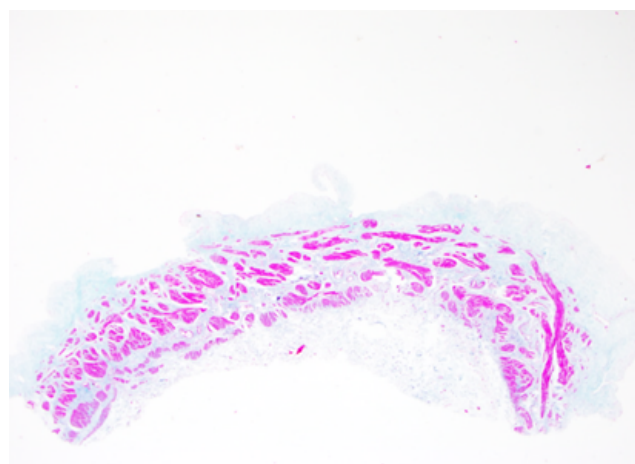


Fig. 4: 2X MT fibrosis of puj segment

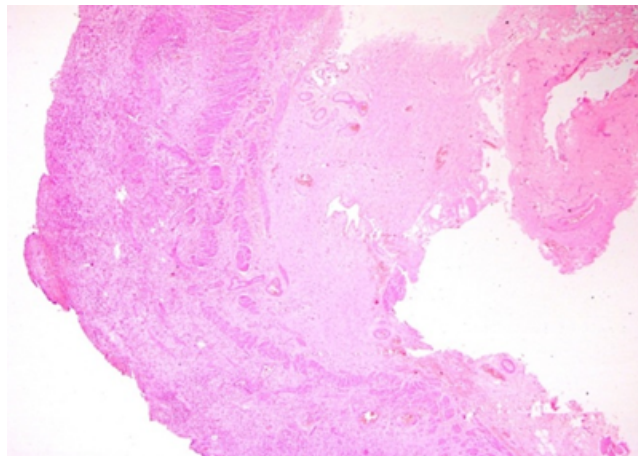


Fig. 5: 2X H & E severe inflammation of puj segment

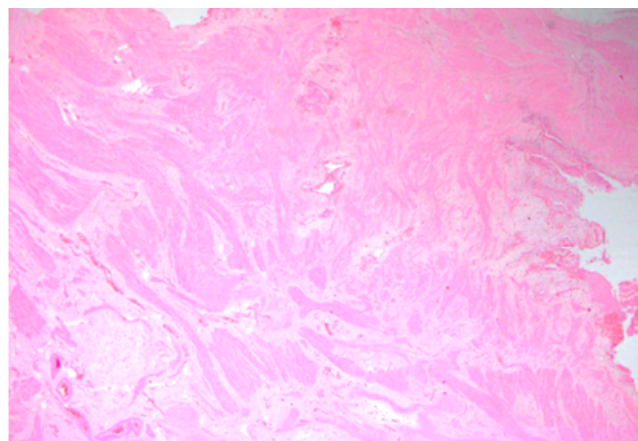


Fig. 6: H&E Muscle Hypertrophy Severe of PUJ Segment

with normal kidneys.¹¹ There is study which shows 19.8% incidence of crossing vessels¹² and 22.22% of incidence⁷. In our study we found crossing vessels in 42 patients out of 128 corresponding to 32.8 % of patients undergoing pyeloplasty.

PUJO, although most often a congenital problem, can present clinically at any time of life. Study by Dogan et al 2017 showed mean age 30.5 ± 18.5 years,¹² In our study we found PUJO in all age groups in both study group, most common being in third decades. It was observed that the mean age clinical manifestation Crossing Vessel group was 29.57 ± 10.50 years while for Non Crossing vessel group the mean age was 30.05 ± 9.94 years.

In our study we found more incidence of disease in males compared to females, It was observed that under the group Crossing level, 71.4% of the patients were males while 28.6% were females. Under the group Non crossing vessel, 62.8% of the patients were males while 37.2% were females. It was observed that under the group Crossing vessel, 66.7% of the patients were diagnosed with R PUJO

while 33.3% were diagnosed with L PUJO. Under the group Non Crossing vessel, 53.5% of the patients were diagnosed with R PUJO while 46.5% were diagnosed with L PUJO. In the literature, it is mentioned that, UPJO occurs more commonly in males than females and the ratio that exceeds 2:13 and left sided lesions predominate (approximately 67%) study by Dogan et al 2017(72.98%) shows lower incidence in females compared to males.¹²

We analysed PUJ segment for presence of inflammation and grade of inflammation, presence of fibrosis and its grade, muscle hypertrophy and its grading, and presence or absence of muscle disarray and synaptophysin.

In crossing vessels groups mild grade inflammation in 76.2% of the patients while moderate to severe grade in 23.8%, mild grade fibrosis in 28.6% of the patients while of moderate to severe grade in 71.4%, muscle hypertrophy of mild grade in 52.4% of the patients while moderate to severe in 47.6%, 28.6% of the patients had Muscle Disarray and 4.8% patients has positive synaptophysin.

In non crossing vessels groups mild grade inflammation in 55.8% of the patients while moderate to severe grade in 44.2%, mild grade fibrosis in 23.3% of the patients while of moderate to severe grade in 76.7%, muscle hypertrophy of mild grade in 69.8% of the patients while moderate to severe in 30.2%, 7% of the patients had Muscle Disarray and 4.7% patients has positive synaptophysin.

Although the crossing vessels group has more higher grade of fibrosis and muscle hypertrophy compared to noncrossing group and noncrossing group shows more higher grade inflammation compared to crossing group these changes were not statistically significant.

Wang et al reported the reduction of neural elements in UPJ obstruction in addition to decreased expression of nerve growth factor, which is important for normal development of axons and establishment of synapsis.¹³

Furthermore, Murakumo et al studied 18 patients, 7 patients in group 1 as control, 4 in group 2 as crossing vessels and 7 patients in group 3 as non crossing vessels group, observed differing nerve distribution between intrinsic and extrinsic UPJ obstruction.⁷

Kazbafzadeh et al studied 23 patients with PUJO with 25 patients of control group, not only have confirmed the preceding reports on the decrease of nerve terminal in obstructed UPJ, but also have shown the correlation between nerve terminal decrement and more myocyte apoptosis and collagen deposition at the site of UPJ obstruction. In addition to increased deposition of collagen fibers, abnormal composition could contribute to ureteral dysfunction at PUJ.¹⁴

Solari et al showed that IC counts decreased in specimens obtained from UPJO group using immunohistochemical methods and antibodies against c-kit. Study compared 19 patients who underwent pyeloplasty due to PUJO and 7 patients in the control group. Study showed, the number

of c-kit positive ICs in the PUJ O group was significantly reduced compared to control group¹⁵

Dogan et al 2017 compared 57 patients in noncrossing vessels Group, 17 patients in crossing vessels Group and 12 patients in normal group. All cases were compared for number of ICs at the level of lamina propria and muscle layer, number of neurons at the level of lamina propria, presence or absence of fibrosis/inflammation. Study find a no significant difference between the three groups in terms of all parameters.¹²

Apoznanski et al. study investigated the ICs of the 20 patients in the intrinsic PUJO group and 5 patients in the control group. They find no statistically significant difference in IC distribution between UPJO and control group.¹⁶

Ozel et al. showed nonspecific evidences of inflammation in the region of UPJO. In our study, we did not find any difference in terms of the presence of inflammation between the groups.¹⁷

7. Conclusion

This study is carried out at tertiary care hospital showing the incidence of crossing vessels in 1/3rd cases (32.8%), indicating that surgeon must be vigilant for the presence of crossing vessels.

On histopathological analysis, the crossing vessels group has more higher grade of fibrosis and muscle hypertrophy compared to noncrossing group and noncrossing group shows more higher grade inflammation compared to crossing group but these changes were not statistically significant.

Based on our findings, we propose that common phenomenon has a role in the pathogenesis of UPJ obstruction whether its associated with crossing vessels or not. We also hypothesised that all of these histological changes inflammation, fibrosis, muscle hypertrophy, muscle disarray and absence of neural tissue together could contribute to failure of transmission of the peristaltic waves across the obstructed PUJ.

The presence of crossing vessels does not lead to any significant change in histopathology of PUJ segment and even in presence of crossing vessels it 's the intrinsic cause of PUJ segment that leading to the disease.

We can conclude based on our study that crossing vessels is the associated finding and not the cause for the disease it 's the intrinsic cause which is responsible for PUJO.

Further studies are needed to elucidate the role of crossing vessels in PUJ obstruction, which could help in the development of new therapeutic modalities.

8. Source of funding

None.

9. Conflict of interest

None.

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