

## Relation between Preoperative vitamin D level and Post operative Infection in Patient undergoing Pancreaticoduodenectomy (Whipple's) procedure

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### ABSTRACT:

*The patient who underwent pancreaticoduodenectomy operation suffers from obstructive jaundice sometimes. Due to lack of bile in intestine these patients have difficulty in absorption of fat soluble vitamin A, D, E and K. Vitamin D has an important role in maintenance of our immune system. So patients who have low serum vitamin D level suffer from infection more than those with normal level in postoperative period. This study aims to identify vitamin D deficiency among patients suffering from obstructive jaundice and see whether they suffer more postoperative infection and hospital stay. In this observational study 13 patients were enrolled after considering the exclusion and inclusion criteria who underwent pancreaticoduodenectomy operation but have low vitamin D level in the department of Hepatobiliary, Pancreatic and Liver transplant Surgery for one year period. Another 13 patients were selected who have normal vitamin D level. They were leveled into two groups. Group one had normal vitamin D level and group two have low vitamin D level. After operation superficial surgical site infection, deep surgical site infection, pneumonia, bile leak, pancreatic fistula, hospital stay were recorded. CRP level were measured on 3rd, 5th and 7th POD. Data analysis to calculate the significance between two groups were done by using SPSS version 23. P value was regarded significant if <0.05. Postoperative infection is significantly lower in normal vitamin D level group. Postoperative CRP level was same on early postoperative period in all patients but in vitamin D normal group CRP level decreases faster. Postoperative hospital stay was shorter in normal vitamin D level group due to less postoperative infection. In conclusion we can say that obstructive jaundiced patient with below normal Vitamin D level prior to pancreaticoduodenectomy surgery have more postoperative infective complications and thus have more hospital stay.*

### Key Words:

Vitamin-D, Pancreaticoduodenectomy, Whipple's, Obstructive jaundice

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## ABSTRACT

The patient who underwent pancreaticoduodenectomy operation suffers from obstructive jaundice sometimes. Due to lack of bile in intestine these patients have difficulty in absorption of fat soluble vitamin A, D, E and K. Vitamin D has an important role in maintenance of our immune system. So patients who have low serum vitamin D level suffer from infection more than those with normal level in postoperative period. This study aims to identify vitamin D deficiency among patients suffering from obstructive jaundice and see whether they suffer more postoperative infection and hospital stay. In this observational study 13 patients were enrolled after considering the exclusion and inclusion criteria who underwent pancreaticoduodenectomy operation but have low vitamin D level in the department of Hepatobiliary, Pancreatic and Liver transplant Surgery for one year period. Another 13 patients were selected who has normal vitamin D level. They were leveled into two groups. Group one had normal vitamin D level and group two have low vitamin D level. After operation superficial surgical site infection, deep surgical site infection, pneumonia, bile leak, pancreatic fistula, hospital stay were recorded. CRP level were measured on 3rd, 5th and 7th POD. Data analysis to calculate the significance between two groups were done by using SPSS version 23. P value was regarded significant if  $<0.05$ . Postoperative infection is significantly lower in normal vitamin D level group. Postoperative CRP level was same on early postoperative period in all patients but in vitamin D normal group CRP level decreases faster. Postoperative hospital stay was shorter in normal vitamin D level group due to less postoperative infection. In conclusion we can say that obstructive jaundiced patient with below normal Vitamin D level prior to pancreaticoduodenectomy surgery have more postoperative infective complications and thus have more hospital stay.

## Introduction

Vitamin D is a well-known regulator of innate immunity (Wei et al., 2015) and it has got a well-known effect on skeletal health (Silvagno et al., 2012). Several studies have shown that vitamin D receptor (VDR) are expressed in platelets, intestines, pancreas and prostate in addition to bone and kidney suggesting that vitamin D control immune function at different cellular level (D'Amelio et al., 2012; Wei et al; 2015; Altieri et al., 2013). It has also been observed that vitamin D and its metabolites enhance

the antimicrobial activities of macrophage and monocytes (Dai et al., 2010). Manal et al. 2018 also demonstrated in their studies that vitamin D increases the chemotaxis and phagocytic activity of innate immune cell. All these studies support the positive role of vitamin D on the immune function of human body. It is a fat soluble vitamin getting absorbed from the intestine in presence of bile (Paula et al., 2014).

Our initial observation is that patient with obstructive jaundice suffer from vitamin D deficiency and its absorption is hampered by the absence of bile in the intestine. In addition to defective absorption, vitamin D deficiency occurs in obstructive jaundiced patient due to less intake of food and less exposure of patient to sunlight during their illness.

Pancreaticoduodenectomy is a complex and major surgical procedure which is offered for most obstructive jaundice patients due to periampullary carcinoma, cholangiocarcinoma affecting lower common bile duct, pancreatic head tumor etc. Few or no attention has been paid to the 'Vitamin D Deficiency' issues during the treatment of obstructive jaundice patients treated by pancreaticoduodenectomy operation. Our insight and correction of the issue may provide useful ways to control infection after the operation.

## Method

After obtaining clearance from the institutional review board of BSMMU this observational study was conducted in our department on the patient who undergone pancreaticoduodenectomy operation for various reasons. The study does not seem to pose any potential risk but the risk related to the operation was discussed with the patients participating in the study. The patients who not consent to participate in the study was assured of being given the same quality of care. All patient with jaundices were included who are above 18 years old and gave consent. Those patients who do not have jaundice were excluded. A data sheet and a consent form were prepared, sample was selected on the basis of inclusion and exclusion criteria, questionnaire was filled with taking informed written consent. Vitamin D was measured before operation. Normal vitamin D level more than 30 ng/ml is set for this study. Patients were divided into two groups after that. Group 1 has normal vitamin D level and Group 2 has vitamin D level lower than 30ng/ml. The primary study end point was the time to discharge to

home postoperatively. Secondary end point was readmission within 30 days of the surgery. Postoperative infective complications, wound infection was identified according to the Centers for Disease Control and Prevention criteria (CDC) guidelines. Appropriate antibiotic was given according to culture and sensitivity. After hospital discharge all patients were followed up in outpatient department from 14-30 post-operative day. Highest level of confidentiality and ethical standard was maintained during storage and analysis of the data. After compilation, the data were presented in the form of tables, figures as necessary. Data analysis was done by statistical software, SPSS 23.0 version. The statistical terms included in this study are mean, standard deviation. Statistical analysis was done by t-test and Chi square ( $\chi^2$ ) test for qualitative variable. Mean and standard deviation of patient age, BMI, and post-operative hospital stay for each group were calculated. Post-operative outcome compared between two groups. Statistical significance was set at p value <0.05.

**Result**

The mean age was found 52.65±10.23 years in group 1 and 54.85±9.91 years in group 2. Male patients were found 5(38.5%) in group 1 and 9(69.2%) in group 2. Females were 8(61.5%) and 4(30.8%) in group 1 and group 2 respectively. The mean BMI was 22.09±3.38 kg/m<sup>2</sup> in group 1 and 21.77±2.70 kg/m<sup>2</sup> in group 2. Age, sex and BMI differences were not statistically significant (p>0.05) between two groups. Regarding the clinical presentations e.g., abdominal pain, itching, weight loss shows that there is no statistically significant (p>0.05) difference between two groups. Post-operative inflammatory status of two groups measured by CRP Level. It shows CRP Level was higher in both groups in POD 3. But it is significantly decreased on POD 5 and POD 7 in Group 1 in comparison to Group 2 patients. Superficial wound infection was found in 46.2% of patients of Group 2 and 15.4% in Group 1. The difference was statistically significant. The Deep Surgical Site Infection was not found in Group 1 in contrast it was in 15.4% patients of Group 2; The difference was statistically significant. There is no Surgical Site Infection in 84.6% patients of Group 1. Pneumonia was significantly higher in group 2 than group 1 (53.8% vs 15.4%). Sepsis was also significantly higher in group 2 than group 1 (15.38% vs 7.69%). Postoperative hospital stay was significantly higher in group 2 than group 1 (25.85±4.54 vs

16.69±4.11 days). Because of post operative infective complications group 2 patient stay for more days.

Table I: Comparison of Demographic Variables and Clinical Presentations between two groups of patients. (n=26)

Variables	Group 1 (n=13)	Group 2 (n=13)	P value
Mean Age (Years)	52.65±10.23	54.85±9.91	0.142 <sup>ns</sup>
Sex			
Male	5 (38.5%)	9 (69.2%)	0.119 <sup>ns</sup>
Female	8 (61.5%)	4(30.8%)	
BMI (kg/m <sup>2</sup> )	22.09±3.38	21.77±2.70	0.789 <sup>ns</sup>
Clinical Presentation	n (%)	n (%)	
Fever	3 (46.2)	2 (15.4)	0.701 <sup>ns</sup>
Itching	7 (53.8)	7 (53.8)	0.652 <sup>ns</sup>
Weight-Loss	7 (53.8)	9 (69.2)	0.344 <sup>ns</sup>
Abdominal Pain	9 (69.2)	7 (53.8)	0.344 <sup>ns</sup>
Duration of Jaundice (Month)(Mean ± SD)	4.85 ± 4.77	6.15 ± 2.88	0.406 <sup>ns</sup>

ns=not significant.

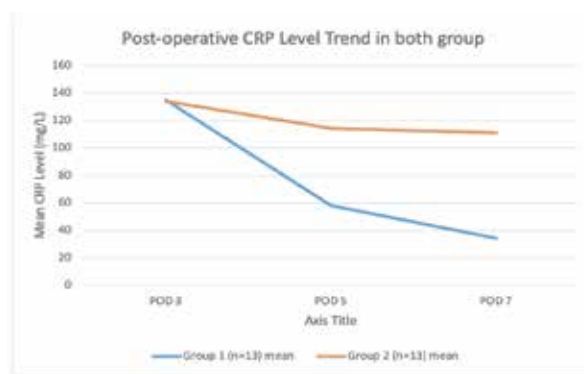


Table II: Distribution of the study population by Infection(N=26)

Surgical site infection	Group 1 (n=13)		Group 2 (n=13)		P value
	N	%	n	%	
Superficial surgical site infection (SSSI)	2	15.4	6	46.2	
Deep surgical site infection (DSSI)	0	0.0	2	15.4	0.044 <sup>s</sup>
No surgical site infection	11	84.6	5	38.5	
Pneumonia	2	15.4	7	53.8	0.049 <sup>s</sup>
Sepsis	1	7.69	2	15.38	0.041 <sup>s</sup>

s=significant

Table III: Distribution of the study population by postoperative hospital stay between two groups (n=26)

Variable	Group 1 (n=13)		Group 2 (n=13)		P value
	mean	±SD	mean	±SD	
Postoperative hospital stays (days)	16.69	±4.11	25.85	±4.54	0.017 <sup>s</sup>

s=significant

## Discussion

Patients with obstructive jaundice invariably suffer from malabsorption of fat soluble vitamins (Altieri et al., 2017). Vit D is directly related to immune modulation. It is a fat-soluble vitamin absorbed from the intestine in presence of bile salts. Several studies have examined the correlation between Vit D concentration and post-surgical infections (Laviano et al., 2020).

The value of perioperative Vit D supplementation has now newly established. But the practice is lacking in Bangladesh. In our study clinical presentation was more or less same in between two groups that were abdominal pain, itching, weight loss and fever. The difference was not statistically significant ( $p > 0.05$ ) between two groups which has similarity with the findings of Murphy et al. (2021) and Tabriz et al. (2021). Patient of both groups had some co-morbidity like diabetes mellitus, hypertension, and chronic obstructive pulmonary disease. Biliary decompression done in some patients to lower the bilirubin level when it is too high. Indication of pancreaticoduodenectomy operation in this study were in order of number of cases are periampullary carcinoma, carcinoma head of the pancreas, distal cholangiocarcinoma, ampullary carcinoma, carcinoma gall bladder and duodenal maltoma.

In this study we assess liver function test preoperatively which include serum bilirubin which is high in both groups. Prothrombin time, INR were similar in two groups. Serum albumin level were low in both groups which was corrected before operation. Difference was not statistically significant between two groups.

Current study we observed that on admission vitamin D level was significantly low in some patients. Because of bile salts lacking vitamin D is not absorbed from intestine and also lack of sunlight exposure due to their illness (Anwar et al. 2018). Before operation vitamin-D level was normal in group 1 than group 2 ( $34.25 \pm 10.91$  vs  $18.27 \pm 5.46$  ng/ml).

Present study we observed that postoperative day (POD) 3 CRP level difference were not statistically significant ( $p > 0.05$ ) between two groups, but significant CRP concentration reduction on postoperative day 5 and 7 occurs in normal group. Tani et al. (2022) observed C-reactive protein (CRP) level on POD 7 were significantly elevated ( $P < .001$  for both) for Vit D deficient

patients. Krasowska et al. (2019) has done such study on PLID operation patients and found similar results.

In this study we observed that superficial site infection was found 2(15.4%) in group 1 and 6(46.2%) in group 2. Deep surgical site infection was 2(15.4%) in group 2, but not observed in group 1. No surgical site infection was 11(84.6%) and 5(38.5%) in group 1 and group 2 respectively. The difference was statistically significant ( $p < 0.05$ ) between two groups. Laviano et al. (2020) observed superficial infection was 3.0%, deep infection 7.0%. The patients with SSI also presented lower concentrations of vitamin D ( $P = .012$ ). Pneumonia was significantly higher in group 2 than group 1 (53.8% vs 15.4%). Sepsis was also significantly higher in group 2 than group 1 (15.38% vs 7.69%). Abdehgah et al. (2019) found increased SSI rate in Vit D deficient patients. Laviano et al. (2020) also found similar findings. Aranow et al. 2011 found that vitamin D has important roles in addition to its classic effects on calcium and bone homeostasis. As the vitamin D receptor is expressed on immune cells (B cells, T cells and antigen presenting cells) and these immunologic cells are all capable of synthesizing the active vitamin D metabolite, vitamin D has the capability of acting in an autocrine manner in a local immunologic milieu. Vitamin D can modulate the innate and adaptive immune responses. Deficiency in vitamin D is associated with increased susceptibility to infection.

In their 2011 review of HAIs and vitamin D serum level, Youssef et al. concluded that patients with vitamin D deficiency had higher rates of infection and that vitamin D level should be checked upon hospital admission to correct insufficiency. In line with the findings of Turan et al. (2014) our results demonstrated an inverse association between the risk of infection and vitamin D serum levels. Moreover, both studies demonstrated an association between higher vitamin D levels and better in hospital outcomes.

In this study observed that postoperative hospital stay was significantly higher in group 2 than group 1 ( $25.85 \pm 4.54$  vs  $16.69 \pm 4.11$  days). As the patient of group 2 suffered from infection they had to stay longer. Some patients needed secondary closure for surgical site infection which prolonged their hospital stay.

## Conclusion:

We conclude that Vitamin D level has a strong effect on postoperative infection in jaundiced patient undergoing Pancreaticoduodenectomy surgery. However study with large sample size and long duration is needed to set a standard protocol for preoperative vitamin D level measurement and correction to reduce postoperative infection.

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