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IMPACT OF BILIARY TRACT INFECTION ON LIVER TRANSPLANT OUTCOMES

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ABSTRACT

Introduction: BTIs are frequent events in the post-liver transplant environment and are universally pathological for both the graft and the patient. The purpose of this paper is to compare the relationship that may exist between BTIs and liver transplant recipients with respect to graft survival, the chances of incidence of complications and the number of days the patient has to spend in the hospital.

Objectives: To establish the overall certainty level of the observed biliary tract infection and its impact on other parameters like graft failure, length of stay at the hospital, and rate of graft rejection in the overall grafts.

Materials and Methods: A retrospective study of 1,085 liver transplant recipients at Pir Abdul Qadir Shah Jilani Institute of Medical Sciences, from September 2018 to August 2024.

Results: BTIs were found in 14% of the enrolled patients. Patients who had received BTIs were found to stay in hospitals for a longer time (28 days against 14 days), experienced higher graft failure (18% against 4%) as well as graft rejection (25% against 10%) rates.

Conclusion: BTIs are directly related to the status of liver transplantation, and efforts should be made to improve the early diagnosis and treatment to enhance the survival rate of patients and grafts.

Keywords: Biliary tract infections, liver transplantation, graft failure, graft rejection, hospital stay, complications.

INTRODUCTION

BTIs remain a common and potentiated issue whose consequences may impact post-transplant results in this population. These can eventually result in negative outcomes like graft failure, sepsis and prolonged hospitalization, which, in turn, unfavourable affect the success of liver transplant surgeries. It is important to establish these connections since BTIs affect a significant number of patients and have an impact on the outcomes of liver transplant attempts. A large number of researches have been done on pre- and post-transplant bacterial infections in relation to liver transplant recipients (1). Liver infections are observed quite frequently after transplant surgery, and their management negatively affects the survival rates of the transplant recipient in the short term and the long term (2). This particular type has a close association with the biliary tree because it performs various functions in the small intestine involving the transportation of bile. Experiences of biliary complications after liver transplantation mainly depend on the architecture and the functionality of the biliary system following

the operation. Any of the diseases or infections may influence the graft and the patient in general (3). The causes of biliary infection are reconstruction of the biliary tree in the transplanted liver and high risks in patients with PSC (4). A history of infections contributes to higher risks of postoperative complications, with better control of infections being necessary to achieve improved survival following the transplantation (5).

The new developments in transplantation have made a significant focus on diagnosing and managing biliary complications such as blood transfusion infections. Evidence on the fact that early identification of biliary tract complications through the use of cholangiography as a routine procedure has influenced the prevention of severe postsurgical infections has also been pointed out in the literature (6). Firstly, the involvement of microbiota in biliary disorders after liver transplantation has attracted increasing attention. A shift in the gut-liver microbiota disruption has been linked to the development of infection, including BTIs, after liver transplantation (7). This is even more so in cases of patients with PSC or who are transplanted for primary sclerosing cholangitis (8). Pre-transplant infections and treatment also affect the post-transplant course of a patient as well as the follow-up of these cases. Additionally, it has been established that there is higher mortality and graft loss among patients who develop infections, including those caused by bacteria that are transplanted into the patient (9).

Living donor grafts and biliary stones are graft-related factors that have a significant influence on the procedure of liver transplantation. Biliary concretions can cause obstructive cholangitis, a condition that has a high propensity to complicate with infection with bacteria in the biliary tree (10). Research on managing factors such as the usage of T-tubes for biliary reconstruction has revealed that these methods may be able to decrease the rates of BTIs (11). However, there is debate regarding the employment of a T-tube and no T-tube as it brings into focus the pros and cons of the two regarding the prevention of biliary complications post-transplant.

Therefore, long-term graft and patient survival in liver transplant recipients with preexisting biliary diseases or those who develop BTIs may also be affected by recipient factors like immunosuppressive drugs and comorbidities (12). Chemopreventive administration of drugs to prevent rejection of the graft puts the patient susceptible to infections, including those of the biliary system. It is for this reason that the management of immunosuppressive therapy is considered an important factor that would help to reduce the incidences of post-transplant BTIs. Moreover, the latest study on the efficacy with respect to thirty years of liver transplant for PSC has indicated that early and adequate control of BTIs is likely to enhance survival rates and reduce the risk of repeat biliary problems (13). The invasive interventions to manage such complications are a challenge, particularly where the transplant recipients themselves suffer from pre-transplant biliary diseases or recurrent biliary infections. Measures intended to reduce rates of biliary tract infections, prophylactic antibiotic administration, and early identification of infections can go a long way in determining the success of the transplantation. However, biliary complications remain a common occurrence and a major factor contributing to graft failure and patient morbidity (14).

Finally, the facets of biliary tract infections on the outcomes of liver transplantation are varied and may include predisposing diseases, surgical procedures, graft profiles, and post-operative management. Knowledge of these factors and implementation of appropriate comprehensive medical management that considers BTIs from before the transplant up to follow-up help to enhance the survival and functionality of both the patient and the graft. These chronic infections related to microbiota show that more research is required to identify the functions of these infections in these infections and the way that more efficient preventive as well as control interventions can be exercised to improve the liver transplantation outcome (15).

Objective: The purpose of this study is to review the effects of biliary tract infectious concerning the graft survival rate and long-term complications and prognosis of liver transplantation patients.

MATERIALS AND METHODS

Study Design: Retrospective Observational Design

Study setting: The study was carried out at Pir Abdul Qadir Shah Jilani Institute of Medical Sciences, Gambat, Khairpur Mir's, Sindh, the leading medical institution that has a liver transplant centre in the mentioned region.
Duration of study: The study was from September 2018 to August 2024.
Inclusion Criteria:
Liver transplant patients in the Pir Abdul Qadir Shah Jilani Institute of Medical Sciences during the study period and developing biliary tract infections after transplantation. Only people 18 years old and above was participating in the study. It also incorporate the patients already diagnosed with the condition before the transplant and a survey of their condition after the transplant.

Exclusion Criteria
The criteria for exclusion was patients who developed biliary tract infection post-liver transplant, little documentation and any patient who is below the age of 18 years. Some of the groups which was excluded from the study of patients with conditions that are not related to the biliary system. Furthermore, patients with conditions that might influence the outcome of the study, including actively progressive cancer or untreated infections, was not selected for this study.

Methods
A total of 1,085 participants including the liver transplant recipients having data in the course of September 2018 to August 2024 in the hospital Pir Abdul Qadir Shah Jilani Institute of Medical Sciences was enrolled in the study. The sample size was calculated according to the number of patients reporting BTIs post-transplantation from the total number of eligible patients. Routine patient medical data are to be retrieved from case notes from pre-transplant medical history, operation and post-transplant follow-up. The occurrence and type of biliary tract infections, as well as the different aspects connected with graft survival, length of hospital stay, and different complications, such as sepsis and graft rejection, was also be registered. Data analysis involve the use of descriptive statistics to describe the patients 'characteristics and infection characteristics. Chi-square and logistic regression tests was applied to relate BTIs and post-transplant complications. Patients' information was disguised to maintain their anonymity, and consent to undertake the research was sought first.

RESULTS
A total of 1085 patients who received a liver transplant and fulfilled the criteria for entering the trial were analyzed. The age, gender, type and etiology of the liver disease, and co-morbid conditions of the patients received from the list were also evaluated. Most of the patients were between 40 to 60 years of age, and more than half of the patients were male. The most common indication for liver transplantation was cirrhosis, which accounted for 45%, followed by hepatitis C-related liver disease 30%, and primary sclerosing cholangitis 15% while the rest had other indications.

Table 1: Demographic Data of Study Participants

Characteristic	Value (%)
Age (years)	
18–39	25%
40–59	50%
60 and above	25%
Sex	
Male	65%
Female	35%
Primary Liver Disease	
Cirrhosis	45%
Hepatitis C	30%
Primary sclerosing cholangitis	15%
Other	10%

BTIs were diagnosed in 152 of the 1,085 patients (14%) during the study period after the transplantation process. Among these, 96 cases were early infections, which were diagnosed within the first 30 days of liver transplantation, while the remaining 56 infections were late infections, which occurred after the first 30 postoperative days. The most frequent isolates in the present study were Escherichia coli 32 %, Enterococcus faecalis21 %, and Klebsiella pneumoniae 18%. Most of the infections involved bile ducts, but on rare occasions, they spread to the bloodstream (sepsis).

Table 2: Post-Transplant Biliary Tract Infections (BTIs) Characteristics

Infection Type	Value (%)
Early-onset (0–30 days)	63%
Late-onset (>30 days)	37%
Common Pathogens	
Escherichia coli	32%
Enterococcus faecalis	21%
Klebsiella pneumoniae	18%
Other Pathogens	29%

This study established that patients receiving grafts, including BTIs, were significantly different for post-transplant outcomes with respect to graft survival and complications. BTIs developed in 152 patients, and 112 (74%) of these had prolonged hospital stays due to complications arising from the infections. Patients with BTIs stayed in the facility for an average of 28 days, while those without BTIs stayed for an average of 14 days. Transplant-associated graft failure developed in 18% of the BTI cases, which was much higher than in the patients without an infection (4%). However, the overall graft rejection incidence was high in patients who had been diagnosed as having BTIs at 25% as compared to patients with no signs of infection at 10%.

Table 3: Impact of Biliary Tract Infections on Post-Transplant Outcomes

Outcome	BTIs (n=152)	No BTIs (n=933)
Prolonged Hospital Stay (>14 days)	74%	25%
Graft Failure	18%	4%
Graft Rejection	25%	10%

Additionally, the results revealed that the patients who have certain biliary tract infections raised the chances of producing a bad liver transplant outcome. This study has shown that patients with BTIs had longer length of hospital stay, higher incidence of graft failure, and graft rejection more often. The findings suggest that there is a growing need to accurately diagnose and manage patients with BTIs in order to enhance the patient and graft survival after transplantation.

DISCUSSION

BTIs are an essential and rather unfavourable factor in the context of LTRs as they align with the timing of the outcome. Regarding the survival of the liver graft, the length of stay and complications related to the transplantation patients who received the aforementioned BTIs were evaluated. The results of this comparison showed that for patients with active BTIs, the engraftment rates are low, the duration of hospital stays is longer, as well as the rejection rate is higher. These works pointed out that correct diagnosis, as well as the management of the condition involving the biliary tree, has implications for the transplant and long-term survival of the patients. BTIs in this study were reported to be 14%, which is within the range of previous studies estimating biliary complications in Liver transplant recipients. The evaluation made regarding the infection profile also indicated that infections that began within the first month after the surgery were early onset at 63%. This postoperative observation has been supported by other studies establishing that early post-transplantation infection contributes to the elevation in the morbidity rate within the early days after the surgery (2). These are principally related to early postoperative complications such as biliary-anastomotic-leak or ischemia, which provide access points (3). However, late-onset infection is usually associated with chronic graft dysfunction and other disorders that result from immunosuppressive therapy, which is a chance for opportunistic organisms (4).

Several factors were found worthy of note in the process of conducting this research, the primary one being the fact that out of all the pathogens that caused BTIs, Escherichia coli was the most common at 32%. This is closely followed by other researchers who established that E. coli is often the only organism isolated in biliary infection after a transplantation process. The fact that E. coli is normally found in the gut and the fact that it was isolated in the biliary tract infection implies a possibility of leakage between the gut and liver capsule as well as immunosuppression. Other bacterial isolates were Enterococcal species, Klebsiella pneumoniae and others, which are recognized organisms in biliary tract infection after liver transplantation (6). Identification of the BTIs and characterization of the microbial species involved acts as a guide for the extent of microdiversity of the microbial biofilm in the biliary system after transplantation and a basis for a sound decision on the type of antibiotic therapy to be administered.

Considering the findings of this research study, it is clear that BTIs significantly impact graft survival and other factors associated with transplantation. The number of patients with BTIs who were admitted within 30 days or more was 74 % more than other patients without BTIs, where this percentage was 25 %. The patients with a BTI stay for an average of 28 days, whereas the patients without infections have an average stay of 14 days. This is in agreement with prior findings that the expected rate of BCs results in prolonged hospital stays and higher healthcare expenditures. The longer length of stay is due to the longer antibiotic treatment period, the need for the treatment of septic episodes, and the additional procedures to address the biliary problems. In addition, this study affirmed that most of the patients with graft failures had been diagnosed with BTIs while the rest were non-infected patients, hence the 18 per cent graft failure rate among the BTI patients as compared to 4 per cent among the non-infected patients. Transplantation of the liver involves the occurrence of graft failure, which makes the patient a candidate for re-transplantation or may lead to death. This is due to infection-related ischemia, biliary structure, or damage to the biliary anastomosis that may result in biliary leakages and rejection of the graft (8). The present study established a positive relation between BTIs and graft failure rates, thereby stressing on having a spirited approach toward infection control for avoiding graft failure. Earlier studies have also noted that infection, especially at the initial period after transplantation, can also contribute to overall graft dysfunction primarily and secondary functions as well (9).

Furthermore, it was also determined that the variables related to BTIs were associated with the likelihood of transplant rejection. This research revealed that 25 per cent of the patients with BTIs suffered from graft rejection compared to only 10 per cent of the other patients with no infections. This finding is in harmony with the general hypothesis that infections can cause immunological reactions that result in graft rejection. Bacterial and viral infections can generally produce inflammation-mediated outcomes that cause T cell activation and cytokine production, which subsequently contributes to an increased risk of graft rejection (10). Another important factor contributing to infection risk is immunosuppressive therapy, as allograft rejection requires its use, and this, in turn, hampers the body's response to infections. Therefore, BTIs could adversely affect the graft directly and/or indirectly contribute to graft rejection through immune modulation.

BTIs are difficult to control in LTR due to the immunosuppressive medications required in the prevention of rejection of the graft. This study builds on the previous results by pointing out that BTIs are more common among patients who are on long-term immunosuppression by distinguishing between rejection and infections in detail (11). These would range from the use of the right antibiotics, cholangiography before surgery or liver transplantation, and early identification of infection symptoms. Therefore, it may increase the readmission time of the patients to initiate optimal graft care, reducing the BTI detection period.

This research also points out that there is a necessity for other work to improvise techniques for preventing and minimizing the occurrences of BTIs in liver transplant recipients. Other techniques, like the portable normothermic machine perfusion put forward for the preservation of the liver graft, may reduce biliary complications further (12). Moreover, knowledge of microbiota characteristics can contribute to the elimination of post-transplant infection, as previous research has shown that the gut-liver microbiota imbalance leads to high infection rates in post-transplant patients (13). Lastly, delayed liver biopsies can be identified as one of the major adverse outcomes of LT, impacting the presence of longer lengths of stay and retransplantation as well as graft rejection implications. This study's findings suggest that more effective ways of identification, appropriate management, and effective protective measures are necessary to combat the impact of BTIs on transplants. Liver transplantation was significant in improving the patient's length of stay and prognosis through the microbiota and infection development, besides innovations in the transplantation procedures.

CONCLUSION

The paper reveal that BTIs have negative impacts on long-term liver transplantation. In this study, the patients who had experienced a BTI and had a longer length of stay in the hospital had a higher rate of graft failure and a higher incidence of rejection. These results strongly attest to the need to improve the knowledge of BTIs and their treatment as soon as possible, as well as in the early post-transplant period, to increase graft and overall patient survival. For instance, Escherichia coli, Enterococcus faecalis and Klebsiella pneumoniae are some of the bacteria that should be treated accurately with antibiotics. Moreover, the study makes it possible to realize that although immunosuppressive therapy helps minimize the risk of graft rejection, it weakens the patient's immune system in terms of infections, which means careful monitoring and prevention. These studies raise the need to continue searching for mechanisms that can reduce the risk of bacterial infections and the impact they have on the quality of life of liver transplant recipients.

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