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SEROLOGIC SUBTYPES OF DQ7 SUGGESTED BY PRINCIPAL COMPONENT ANALYSIS OF SINGLE ANTIGEN SCREENING DATA

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Objective: It is routine practice to test patient serum for antibodies using single HLA antigens as targets. WHO serologic specificities are currently used to specify patient antibodies. Investigators have found sera which appear to react selectively with one or more alleles within a WHO specificity, but these have not been well defined. Methods for systematically searching for such new antibody specificities are needed.

Methods: We analyzed 2750 sera from 1215 patients awaiting a solid organ transplant on class II single antigen beads (one lambda) using a Luminex platform. We used principal component analysis (PCA), a statistical method to find distinct patterns in multivariate space which account for the observed data.

Results: For sera tested on the five DQ7 beads, three principal components accounted for 99.3% of the data variance. The first component represented the 88.8% of sera which reacted equally with all of the five alleles. The second component accounted for 9.2% of the data in which (DQA*03:01, DQB*03:01) has a distinct pattern of reactivity from the other alleles. The third component accounted for 1.3% of the data variance, were sera in which (DQA*03:03, DQB*03:01) had a unique pattern of reactivity (Table 1).

Conclusions: PCA is a powerful tool to identify candidate sera which can be used to detect new serological specificities and might yield new WHO antigen definitions. The data suggests three serologic subtypes within DQ7.

Table 1: Allele factors contributing to three main DQ7 principal components

HLA Target	Component 1	Component 2	Component 3
DQA1*03:01, DQB1 *03:01	0.37	0.91	0.17
DQA1*03:03, DQB1 *03:01	10.46	-0.04	-0.87
DQA1*06:01, DQB1 *03:01	10.47	-0.14	0.09
DQA1*05:03, DQB1 *03:01	0.46	-0.27	0.33
DQA1*05:05, DQB1 *03:01	0.46	-0.29	0.32

IS PHARMACOLOGICAL PRETREATMENT DECREASE ISCHEMIC REPERFUSION INJURY OF THE LIVER?

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Background: Although many advances have been made in liver transplantation, ischemic reperfusion injury of the liver remains one of the challenging problem in liver surgery.

Objective: The purpose of this study was to investigate the effectiveness of the Essensiale-forte (EF) on ischemic reperfusion injury of the liver.

Methods: All experiments were performed according to Bashkent University Medical Faculty guidelines for the care and use of laboratory animals. The study animals were age-matched male Sprague Dawley rats weighing 250–300 g. Animals were housed in individual polymethyl methacrilate cages, with free access to food and water before, during, and after the I/R procedure. Light (from 8:00 to 19:00) and room temperature (21–2 °C degree) were kept constant. 48 male rats were randomly divided into 6 groups. There were 8 rats in each group. Group 1 was the control group. Group 2 rats were pretreated with EF (20 mg/kg im), two days before experiments. In group 3 rats we created ischemic reperfusion model. Group 4 rats were received 20 mg/kg EF and I/R were performed. In group 5, after I/R, liver resection was made. Group 6 rats were pretreated with EF; I/R followed by liver resection were performed. After the experiments, blood samples were drawn from the inferior vena cava and rats were sacrificed. Additionally, to determine the level of the tissue damage, liver tissue was taken for morphological and TUNEL study.

Results: ALT, AST, ALP, TNF-α, and MDA level were significantly lower in groups 1, 2, 4, and 6 than those in groups 3 and 5. Moreover, in comparison to groups 1 and 3, NO level was higher in groups 2, 4, 6. Histological examination showed that sinusoidal damage as well as necrotic areas and apoptotic sinusoidal endothelial cells were lower in groups 2, 4 and 6 than in groups 3 and 5.

Conclusion: EF pretreatment protects liver from I/R injury through multiple pathways, regulates multiple bioactive molecule expression and activity, and inhibits cell apoptosis and neutrophil infiltration.

COMPLICATIONS OF OPEN LIVING DONOR NEPHRECTOMY: A REVIEW OF 10-YEAR EXPERIENCE

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Background: Open living donor nephrectomy has brought hope for many patients suffering from 3 hours a day, 3 times a week hemodialysis—the hope of getting rid of being dependent on these large machines. However this technique has its own complications and risks for the kidney donors.

Objectives: In this study, we reviewed complications of this technique during last 10 years.

Methods: We reviewed the operative complications of open living donor kidney transplantations during the last 10 years.

Results: Of 761 kidney donors, 523 (68.7%) were male and 238 (31.3%) were female. Donated side was 181 (23.8%) kidneys from the right side and 580 (76.2%) from the left side. We had no case of mortality from open kidney donation during this 10-year period. Operative or post-operative bleeding necessitating blood transfusion occurred in 27 (3.5%) cases. Pleural injury happened in 27 (3.5%) of cases, of which 3 (0.4%)

cases needed chest tube placement. Post-operative fever was seen in 53 (7.0%) cases of whom 12 (1.6%) stayed in the hospital for more than 5 days. The mean operative time was 138.4 minutes.

Conclusion: Living kidney donation is associated with low surgical morbidity and mortality, while it is donation of freedom from dependence to machinery dialysis and its complications.

THE EFFECT OF DIABETES MELLITUS ON PATIENTS AND GRAFT OUTCOMES AFTER KIDNEY TRANSPLANTATION

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Objective: This study was conducted to determine the differences between diabetic and non-diabetic renal transplant recipients.

Methods: 252 kidney transplant recipients who underwent kidney transplantation in Baqiyatallah Hospital between March 2007 and September 2009 were retrospectively studied. Patients were divided into two groups: non-diabetics (Non-DM) and diabetics (DM). The median follow-up was 29 months. Diabetes were define according to the American Diabetes Association (ADA) criteria. Diabetes was considered if the fasting blood glucose was ≥126 mg/dL confirmed by repeated tests. Graft loss was defined as "need to dialysis for renal replacement therapy." The overall patient and graft survival rates were calculated using the Kaplan-Meier survival analysis. The log-Rank test was used to determine statistical differences in survival rates between the two groups. Multivariate analysis was done by the Cox proportional hazard model for patient and graft outcomes.

Results: DM was seen in 46% of recipients, whereas 182 of them received kidney from living donors (11% living related and 89% living unrelated) and 70 from deceased donors. The majority of patients were first kidney transplantation (n=239, 94.8%), while second transplantation was done in 11 (4.4%) of cases and third kidney transplantation was only performed in 2 (0.8%) of patients. The first and re-transplantation were not significantly different between both groups (p=0.09). Patients who had DM were significantly older at the time of transplantation. Renal function was remained among the DM patients the same as the Non-DM cases (median serum creatinine 1.35 mg/dL *vs* 1.30 mg/dL, p=0.8). No significant differences were observed between the two groups in terms of patient and graft survivals. Multivariate analysis by Cox regression showed that age and gender of recipient, donor source and DM had no adverse effects on short-term outcome among our patients.

Conclusion: We found that DM had no significant influence on patient and graft survival.

OUTCOME OF KIDNEY TRANSPLANTATION IN PEDIATRIC KIDNEY RECIPIENTS

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Objectives: To determine the morbidity and graft survival rate in kidney recipients aged between 6 and 18 years who had undergone kidney transplantation in Imam Reza Hospital, Mashhad, northeastern Iran during 1992-2009.

Methods: Of 1585 kidney recipients who had undergone kidney transplantation in our center during 1992-2009, 168 patients aged from 6–18. Neurogenic bladder, reflux nephropathy, posterior urethral valve,

prunebelly syndrome and chronic glomerulonephritis were diagnosed to be the cause of renal failure in these patients. 22% of the donors were related living, 66% were unrelated living and 12% were cadaveric. Immunosuppressive therapy was initiated with cyclosporine, mycophenolate mofetile, azathiporine and prednisolone. Kaplan-Meier survival analysis was used to assess graft and patient survival while log-Rank test was used to assess the effect of kidney source and the time of renal transplant.

Results: All the studied patients developed immediate diuresis. Surgical complications included 2 urinary fistulas, 2 ureteral strictures and 3 clinical lymphoceles all of which were surgically managed. Chronic rejection and recurrence of the underlying renal disease were the most common cause of graft loss. Graft survival rate after 1, 2, 5, and 10 years of kidney transplantation were 97%, 88%, 79%, 65% and 53%, respectively.

Conclusion: Kidney transplantation in children results in physical growth improvement and mental development. Graft survival rate due to chronic rejection, underlying kidney disease recurrence and incompliance in taking medicines remain to be a problem.

NATIVE NEPHRECTOMY IN PREPARATION FOR PEDIATRIC KIDNEY TRANSPLANTATION

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Background: Indications for native nephrectomy in patients with end-stage renal disease (ESRD) prior to kidney transplantation (KT) are not well defined. Malfunctioning kidneys are removed if they are perceived to pose short- or long-term risks to the KT recipient and/or allograft.

Objecvtive: The aims of this retrospective, single-center cohort study were to evaluate 1) indications, surgical approach and morbidity of peri-transplant native nephrectomy in children, and 2) effects of nephrectomy on clinical and biological parameters.

Methods: Between 1992 and 2010, 49 (41%) of 119 consecutive pediatric transplant recipients underwent unilateral (one-third) or bilateral nephrectomy.

Results: 47% of patients had underlying anomalies of the kidney(s) and urinary tract, 22% cystinosis, 12% focal segmental glomerulosclerosis and 6% congenital nephrotic syndrome. Main nephrectomy indications were polyuria (25%), large proteinuria (20%), polyuria and large proteinuria combined (18%), and recurrent urinary tract infection (23%). Clinically important complications, including peritoneal laceration, were documented in 10%. In polyuric and proteinuric patients, respectively, urine output decreased from a median of 3.95 to 2.26 mL/kg/h (-30%) and proteinuria from 160 to 100 mg/h/m^2 (-40%) after unilateral nephrectomy (p=0.002). Bilateral nephrectomy normalized serum albumin, total protein and fibrinogen concentrations in 90%, 75% and 50% of patients, respectively. The incidence of graft thrombosis (2%–3%) or early graft loss (6%) was similar in nephrectomized and non-nephrectomized cohorts.

Conclusion: Unilateral and bilateral peri-transplant nephrectomies are generally well tolerated with acceptable surgical risks and morbidity. Unilateral nephrectomy satisfactorily reduced urine volume, but not nephrotic-range proteinuria. Severe protein loss requires bilateral nephrectomy to normalize serum protein levels.

SMALL BOWEL AUTOTRANSPLANTATION FOR LOCALLY ADVANCED CARCINOMA OF THE PANCREAS AND RETROPERITONEAL RHABDOMYOSARCOMA: OUR EXPERIENCE IN SEVEN PATIENTS

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Background: Resection is the treatment of choice for adenocarcinomas of the pancreas and some other retroperitoneal tumors, but once the mesenteric pedicle is involved by the tumor it is impossible to perform a free margin resection. Total abdominal exenteration and *ex-vivo* resection of the tumor is a new technique for treatment of these locally advanced tumors.

Methods: From August 2010 to April 2011, 6 patients with preoperative diagnosis of locally advanced pancreatic carcinoma and one patient with retroperitoneal rhabdomyosarcoma treated with en-bloc resection of the tumor and small bowel autotransplantation following *ex-vivo* resection of the tumor. The patient demographics are listed in Table 1. Immunosuppressive regimen consisted of low-dose Tacrolimus for patients in whom autologous vein graft was used for hepatic arterial reconstruction.

Results: The first case died 8 months after transplantation of sepsis. One patient died in hospital of post-operative multi-organ failure. Other patients survived the procedure and are followed for 1 to 6 months.

Conclusions: Although small bowel autotransplantation following *ex-vivo* resection of the locally advanced pancreatic carcinomas and some retroperitoneal tumors may increase the resectability rate, the effect of this technical advance on the survival rate of the patients is not clear.

Table 1: Patient demographics

Age	Pre-operative diagnosis	Post-operative diagnosis	Resections	Tx*
56	Pancreatic carcinoma	Pancreatic carcinoma	Total pancreaticoduodenectomy; total gastrectomy; splenectomy; Right hemicolectomy	Small bowel
52	Pancreatic carcinoma	Pancreatic carcinoma	Total pancreaticoduodenectomy; Right hemicolectomy;	Small bowel
58	Pancreatic carcinoma	Tissue reaction due to previous ruptured teratoma	Total pancreaticoduodenectomy; total gastrectomy; hepatectomy; splenectomy; Right hemicolectomy	Small bowel and liver
32	Pancreatic carcinoma	Pancreatic carcinoma	Total pancreaticoduodenectomy; total gastrectomy; splenectomy; Right hemicolectomy	Small bowel
45	Pancreatic carcinoma	Pancreatic carcinoma	Total pancreaticoduodenectomy; total gastrectomy; splenectomy; Right hemicolectomy	Small bowel
47	Pancreatic carcinoma	Chronic pancreatitis with sever fibrosis	Left nephrectomy;	Small bowel
16	Retroperitoneal rhabdomyosarcoma	Retroperitoneal rhabdomyosarcoma	Total pancreaticoduodenectomy; total gastrectomy; Right hemicolectomy	Small bowel

*Tx: Transplantation

ASSOCIATION BETWEEN TACROLIMUS CONCENTRATION AND GENETIC POLYMORPHISMS OF CYP3A5 AND MDR1 DURING THE EARLY STAGE AFTER LIVER TRANSPLANTATION IN IRANIAN POPULATION

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Background: Tacrolimus (FK506) is widely used as an immunosuppressive drug in liver transplant recipients with a narrow therapeutic range and variable individualized pharmacokinetic. Tacrolimus is a substrate of cytochrome P-450 (CYP) 3A enzyme and the drug transporter ABCB1.

Objective: We have determined the genotypic frequencies of CYP3A5 and ABCB1 single nucleotide polymorphisms (SNPs) in a population of 100 Iranian liver transplant patients and also investigated the influence of the above-mentioned SNPs on tacrolimus concentrations.

Methods: At 7 and 30 days after liver transplantation, tacrolimus doses (mg/kg/day), trough blood levels (T0) and dose-adjusted concentration (concentration/dose ratio) were determined in 100 Iranian patients. Polymerase chain reaction followed by restriction fragment length polymorphism analysis was used for genotyping CYP3A5*3 [6986A>G] as well as ABCB1 [3435C>T].

Results: 95% of the population showed a CYP3A5*3/*3 genotype. ABCB13435TT genotype was observed in 33(33%) cases; whereas 51 (51%) cases carried 3435CT and 16 (16%) cases carried 3435CC. With regard to the ABCB1and CYP3A5, they did not show any influence on tacrolimus dosing requirements in either 1 week or 1 month after transplantation. Also, there was no association of any genetic variant with the acute rejection rate.

Conclusion: Pharmacogenetics profiling of FK506 is not recommended for personalizing immunosuppressive therapy in Iranian population.

HYPERGLYCEMIA AFTER RENAL TRANSPLANTATION: Frequency and Risk Factors

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Background: Chronic renal failure is an important and common complication of diabetes mellitus. Therefore, renal transplantation is a frequent and the acceptable treatment in patients with diabetic nephropathy requiring renal replacement therapy. On the other hands, renal transplantation and its conventional treatment can lead to increased diabetes outbreak in normoglycemic recipients. Also, uncontrolled hyperglycemia may increase allograft loss and decreased patient survival.

Objective: To assess the frequency of hyperglycemia in transplant patients and its risk factors.

Methods: A large retrospective study was performed in 3342 adult kidney transplant recipients between 2008 and 2010. Demographic and laboratory data gathered for each patient. All tests were done in a single laboratory. Hyperglycemia was defined as fasting plasma glucose >125 mg/dL. Univariate and multivariate logistic regression analyses were used to determine the risk factors of hyperglycemia following kidney transplantation.

Results: There were 2120 (63.4%) men and 1212 (36.3%) women. The prevalence of hyperglycemia was 22.5%. By univariate linear regression, hyperglycemia was significantly higher in patients with CMV infec-

tion (p=0.001), elevated serum creatinine (p<0.001), low HDL (p=0.01), and increased blood levels of cyclosporine (p<0.001). After adjusting for covariates by multivariate logistic regression, the hyperglycemia rate was significantly higher for patients with cyclosporine trough level >250 (p<0.001), serum creatinine >1.5 (p<0.001) and HDL <45 (p=0.03).

Conclusion: Hyperglycemia is a common metabolic disorder in Iranian kidney transplant patients. Risk factors for hyperglycemia were higher cyclosporine level, impaired renal function, and reduced HDL value.

SYSTEMIC FUNGAL INFECTION IN LIVER TRANSPLANT PATIENTS IN IRAN

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Background: Systemic fungal infections caused by opportunistic mycoses are grave complications with high mortality rates in liver transplant recipients. Candida spp. and Aspergillus spp. are the most etiologic agents of invasive fungal infections in immunocompromised individuals, and the major causes of morbidity and mortality among the organ transplant recipients.

Objective: In this study, the incidence of invasive fungal infections was evaluated in liver recipients, in Shiraz, Iran.

Methods: From March 2009 to July 2010, 259 recipients undergone liver transplantation were followed and evaluated for fungal infections by microscopic examination, culture of clinical samples, and real-time PCR in serum samples, at Nemazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Blood samples were cultured by bedside inoculation to BACTEC medium.

Results: Of the 259 liver recipients, 158 (61%) were male and 101 (39%) female. The lower limit of detection for this PCR assay was one colony-forming unit/mL of serum. Fungal infections were diagnosed in 27 patients (10.4%), with clinical and radiological signs, including aspergillosis 12 (4.6%) and candidiasis 15 (5.8%). The median time to diagnosis was 21 days. There were 11 women and 16 men with a median age of 42 (range: 17–47) years.

Conclusion: Epidemiology of fungal infection in the liver recipients could help promote the survival through the better management of their conditions and taking preventive strategic measures. In doing so, careful surveillance and reports can be suggestive of the prioritization of research studies and supportive efforts.

THE EFFECTS OF LATE UROLOGICAL COMPLICATIONS ON GRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION IN LIVING AND CADAVERIC DONORS

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Objective: The aim of this study was to evaluate graft survival after treatment of late urological complications (UC) in living and cadaveric donors.

Methods: Between April 1980 and April 2010, 1443 recipients received a kidney transplant (1152 from living donors and 291 from cadaveric donors). We assessed UC which occurred 3 months after transplanta-

tion retrospectively. In total, 41(2.8%) late complications were recorded. Ureteral stenosis (n=26, 1.9%), symptomatic vesicoureteral reflux (n=4, 0.3%), calculi (n=11, 0.8%). Ureteral stenosis corrected surgically by ureteroneocystostomy, ureteropyelostomy. Ipsilateral pyelopyelostomy and contralateral native pyelopyelostomy. Urinary calculi treated by ESWL or urological procedures.

Results: No peri- or post-operative complications or recurrence or graft loss were seen after these interventions. Late UC rates in recipients from living and cadaveric donors were 1.7% and 2.9%, respectively (p=0.072). There was no significant difference in graft survival between recipients with and without late UC (p>0.05).

Conclusion: Although late complications are more common in cadaveric than living kidney transplants, by accurate diagnosis, early invitation and surgical experience, the graft survival will be the same in both groups and in this way, morbidity, mortality and graft loss can be prevented.

HYPERURICEMIA AFTER RENAL TRANSPLANTATION

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Background: Hyperuricemic patients have been predisposed to cardiovascular disease, hypertension, and renal disease. Hyperuricemia is implicated in endothelial dysfunction and in increased production of inflammatory mediators including C-reactive protein.

Objective: To evaluate the prevalence of hyperuricemia and its risk factors among renal transplant recipients.

Methods: A retrospective observational study was conducted among 4217 renal transplant recipients between April 2008 and January 2011. All patients referred from different kidney transplant centers, Tehran, Iran to a single laboratory. The mean±SD age of transplantation was 5±4 (median: 4.2) year. During this period, uric acid was measured in 17,686 blood samples of 4217 renal transplant recipients (64% male and 36% female). Hyperuricemia was defined as a serum uric acid (SUA) level ≥7.0 mg/dL in males and ≥6.0 mg/dL in females that persisted for at least two consecutive tests performed. Moderate to severe hyperuricemia was also defined as a SUA level ≥8.0 mg/dL. Multivariate regression analysis was used for identifying risk factors for hyperuricemia.

Results: The median age of recipients was 38 years. The majority of cases were male (63%). The median age of the donor was 28 years. The majority of grafts came from living donors (84.6% unrelated and 7.8% related), whereas 7.6% of patients received a deceased donor graft. We found that 1340 (31.8%) of recipients had hyperuricemia. Moderate to severe hyperuricemia was observed in 572 (13.6%) of patients. Although hyperuricemia was frequently occurred in women (34% in women *vs* 25% in men, p<0.001), the rate of moderate to severe hyperuricemia was higher in men compared to women (15.5% *vs* 10.3%, p<0.001). There was a significant relationship between SUA and serum creatinine (p<0.001) as well as cyclosporine levels (p<0.001). In multivariate logistic regression, we found that, the increased trough level of cyclosporine was a risk factor of hyperuricemia.

Conclusion: Since hyperuricemia is frequently seen in renal transplant recipients and high level of cyclosporine is the most important risk factor for developing hyperuricemia, the effective treatment would be cyclosporine dose reduction as much as possible.

ANXIETY AND DEPRESSION: A COMPARISON BETWEEN LIVING AND CADAVERIC RENAL TRANSPLANT RECIPIENTS

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Background: Anxiety and depression are the most common psychological disorders in the kidney transplant recipients that may affect disease process and graft survival.

Objective: Based on the types of kidney donation in our country, living *vs* cadaveric donation, we designed this study to compare psychological problems in renal recipients.

Methods: This cross-sectional study was done in kidney transplant recipients who were categorized according to the type of their donors into living and cadaveric groups. Patients with stable condition entered the study; all of them had gone to outpatient clinics for monthly visit. The psychological status of each patient was assessed by a clinical interview and Spielberg State Trait Anxiety Inventory and the Beck Depression Inventory (BDI). Cronbach alpha reliability for the total scale was 0.95.

Results: We recruited 120 recipients (60 patients in each group of living and cadaveric donor transplantation) into the study. There was no significant difference in demographic data between the two studied groups ($p>0.05$). The mean±SD anxiety score was significantly lower among living transplant recipients compared with cadaveric transplant recipients (80.2±15.2 *vs* 86.9±18.8, $p=0.03$). We also found significant relation between mean±SD depression score and kind of graft donation in the studied patients (11.6±5.7 in living *vs* 16.4±9.4 in cadaveric recipients, $p<0.005$).

Conclusion: Periodic psychologic evaluation should be recommended for kidney transplant recipients, especially in cadaveric group.

NEW-ONSET DIABETES MELLITUS AFTER LIVER TRANSPLANTATION

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Background: New-onset diabetes mellitus (NODM) is a serious complication after liver transplantation that may affect graft function and survival of patients.

Objective: This study was conducted to evaluate risk factors of NODM in liver transplant patients.

Methods: A case-control study was conducted in Transplant Center of Shiraz University of Medical Science in March 2011. Patients with NODM after liver transplant were compared to those liver transplant patients without progression of diabetes mellitus after transplantation.

Results: 23 patients (17 men and 6 women) among 200 patients developed NODM after liver transplantation. These patients were compared with 23 (14 men and 9 women) liver transplant patients without diabetes. The mean±SD age of patients who developed NODM was 42.3±9.4 years while it was 32.2±10.0 years in non-diabetics ($p=0.001$). The mean±SD weight of NODM patients before transplantation was 68.4±14.0 *vs* 63.7± 8.8 kg in non-diabetics ($p=0.17$). The mean plasma fasting glucose before liver transplantation was significantly higher in NODM patients compared to non-diabetics ($p=0.002$) (93.9±16.8 *vs* 80.0±10.1 mg/dL). Patients who developed NODM after liver transplantation received higher dose of tacrolimus as immunosuppressive medication than non-diabetics ($p=0.001$).

Conclusion: Older patients and patients with higher fasting plasma glucose level are prone to NODM after transplantation. Higher dose of tacrolimus is associated with development of diabetes after liver transplantation.