OBESITY AND TRANSPLANTATION

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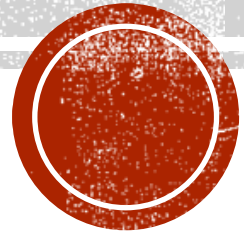

OBESITY AND CKD AND RENAL TRANSPLANT IN PEDIATRIC POPULATION

- In the past several years, obesity in children and adolescents has become a major concern for pediatricians. Although most children with kidney failure are not overweight, increasing numbers are obese when dialysis or transplantation is initiated
- Obesity develops at a significant rate in pediatric patients after renal transplantation
- The presence of obesity and metabolic syndrome in the pediatric CKD and transplant population may augment the already increased cardiovascular risk and contribute to the loss of kidney function
- The Pediatric Renal Nutrition Taskforce is an international team of pediatric renal dietitians and pediatric nephrologists who develop clinical practice recommendations for the nutritional management of children with kidney diseases

Assessment and management of **obesity** and metabolic syndrome in children with CKD stages 2-5 on dialysis and after **kidney transplantation**-clinical practice recommendations from the **Pediatric Renal Nutrition Taskforce**. Stabouli S et al.Pediatr Nephrol. 2022 Jan;37(1):1-20.

DEFINITION

Overweight and Obesity

- **2–5 years:**
- **Overweight** - weight-for-height for age > +2SD, using the World Health Organization (WHO) child growth standard chart.
- **Obesity** - weight-for-height for age > +3SD, using the WHO.
- **> 5 years:**
- **Overweight** - BMI for age > +1SD, equivalent to BMI > 25 kg/m2 at 19 years, using the WHO growth reference chart or a country specific growth chart.
- **Obesity** - BMI for age > +2SD, equivalent to BMI > 30 kg/m2 at 19 years

Metabolic syndrome

- **2–18 years:**

Presence of overweight/obesity and at least 2 of 4 additional CV risk factors:

- **Systolic and/or diastolic** office blood pressure (BP) ≥ 90th centile for age, sex and height or ≥ 130/80 mmHg, which ever is lower, or on anti-hypertensive medication
- Fasting **triglycerides** ≥ 100 mg/dL (1.1 mmol/L) if age < 10 years, or ≥ 130 mg/dL (1.5 mmol/L) if age ≥ 10 years
- Fasting high-density lipoprotein (**HDL**) < 40 mg/dL (1.03 mmol/L)
- Fasting serum **glucose** ≥ 100 mg/dL (5.6 mmol/L) or known type 2 diabetes mellitus (T2DM)

PREVALENCE

- The prevalence of overweight in pediatric renal transplant recipients is notably high and tends to increase post-transplantation.
- Plumb et al., 31.4% of pediatric patients (159 patients, 56<5yrs)- overweight or obese pre-transplantation, which increased to 52.8% in 4 year follow-up period.
- Bondi et al. 25% of pediatric solid-organ transplant recipients (410 children, median transplant age -8.9yrs), developed obesity within 5 years post-transplant.
- Taner et al. - prevalence of overweight and obesity increased from 9% at the time of transplantation (total 136 pts) to 31.6% two years post-transplantation.

- **Longitudinal Changes in Body Mass Index Following Renal Transplantation in UK Children.**
  Plumb LA, et al. Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2014;29(1):196-203
- **Incidence and Risk Factors of Obesity in Childhood Solid-Organ Transplant Recipients.**
  Bondi BC, et al. Transplantation. 2020;104(8):1644-1653.
- **Effects of Body Mass Index Changes in Pediatric Kidney Transplant Patients.**
  Taner S, et al. Transplantation Proceedings. 2023;55(5):1111-1115.

Complications

1. **Delayed graft function (DGF)**: Overweight and obese pediatric renal transplant recipients have a higher risk of DGF.
2. **Acute rejection**: The risk of acute rejection was found to be increased in overweight and obese pediatric patients.
3. **Prolonged hospitalization**: more likely to experience prolonged hospital stays post-transplantation (OR 1.35, 95% CI 1.17-1.54).
4. **Graft failure**: Increased hazard of graft failure. (HR of 1.13-1.61 (95% CI 1.05-1.22) for graft failure in obese pediatric recipients).
5. **Mortality**: Associated with higher mortality rates in pediatric renal transplant recipients. (HR 1.19, 95% CI 1.05-1.35).
6. **Cardiometabolic risks**: Higher cardiometabolic risks, including increased leptin levels, lower HDL cholesterol, higher free fatty acids, and higher glucose levels.
7. **Surgical complications**

- Outcomes of Underweight, Overweight, and Obese Pediatric Kidney Transplant Recipients.
  Kaur K, et al. Pediatric Nephrology (Berlin, Germany). 2018;33(12):2353-2362.
- Obesity in Pediatric Kidney Transplant Recipients and the Risks of Acute Rejection, Graft Loss and Death.
  Ladhani M, et al. Pediatric Nephrology (Berlin, Germany). 2017;32(8):1443-1450.

Cardiometabolic Risks Vary by Weight Status in Pediatric L
Recipients: A Cross-Sectional, Single-C
He S, et al. Pediatric Transplantation. 2017;

- 80 adolescents kidney (63) or liver (1
- Mean±SD, 14.8 years ±3.0
- Mean duration from transplant of 6.0 (
- 32.5% of participants were OW
- Higher leptin,
- lower HDL,
- higher free fatty acid,
- higher apoB-to-apoA1 ratio,
- higher glucose
- Regardless of obesity status, 57.5%of metabolic risk using consensus guide
- While overweight and obese weight s dichotomizing the patients by weight patients were more likely to have mul normal weight children after transpla

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WILEY

in pediatric kidney
onal, single-center

R. Jin[3] | R. Liverman[4] |

term metabolic changes and resultant
asing after pediatric kidney and liver
and novel cardiometabolic biomarkers
nsplant recipients. We enrolled a total
nsplant recipients (63 kidney, 17 liver)
(±4.1) years. Among kidney transplant
ad higher leptin (16.7 vs 7.5 μg/mL,
igher free fatty acid (0.6 vs 0.5 mmol/L,
5, *P*=.03), and higher glucose (5.8 vs
normal weight individuals. Regardless
7.5%) were considered at high cardio-
this was more pronounced for kidney
on adolescents have increased cardio-
factors of obesity and diabetes. The
arkers of cardiometabolic risk. Future
esity can improve the health and long-

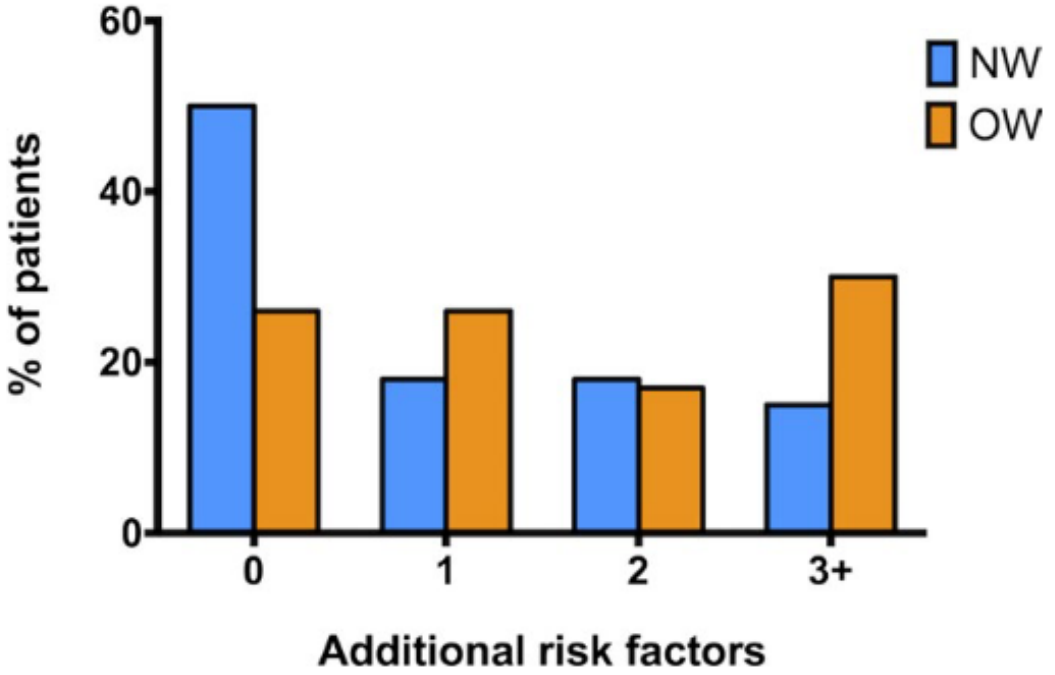

FIGURE 1 Percentages of kidney transplantation recipients with 0, 1, 2, and 3+ cardiovascular risk factors by weight categories. OW=overweight or obese; NW=normal weight or underweight. This graph presents the percentages of kidney transplant recipients with different numbers of risk factors, from none to more than three. Percentages are within each weight category (for OW or NW, respectively). The following cardiovascular risk factors were counted: total cholesterol ≥5.18 mmol/L (age <20 y), or ≥5.83 (≥20 y); LDLc ≥3.37 mmol/L (<20 y), or ≥4.14 (≥20 y); triglycerides ≥1.13 mmol/L (0-9 y), or ≥1.47 (≥10 y); HDLc ≤1.04 mmol/L (all ages); fasting glucose >6.99 mmol/L (all ages)

WEIGH

- **Weight loss**
  significant
- Grèze et al.
  with improv
- Patient surv
  1.23).
- Graft surviv
- Survival rat
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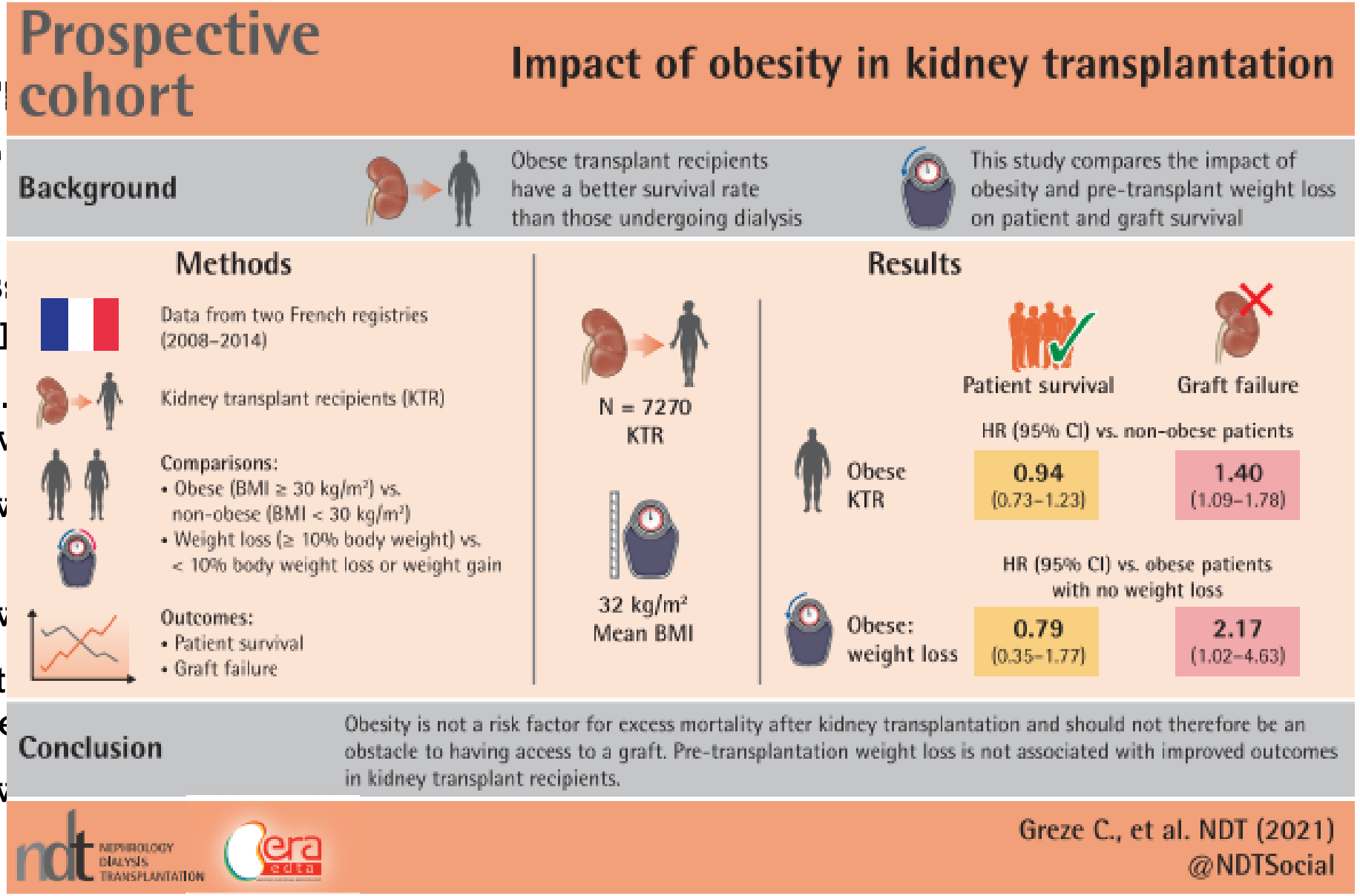
- Graft surviv

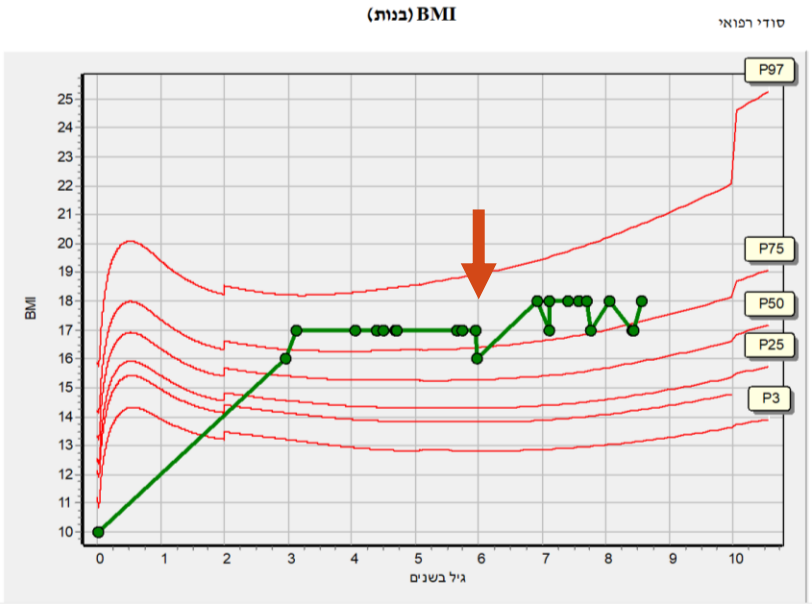


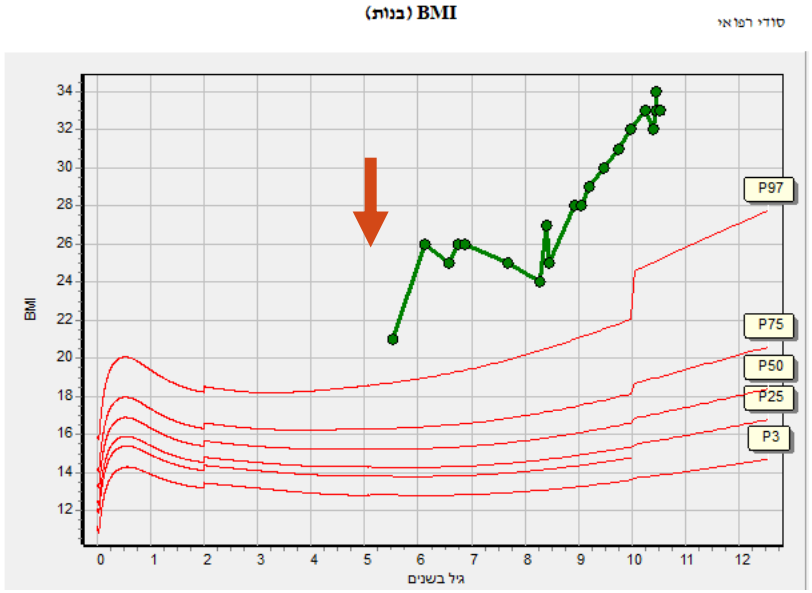
IMPACT OF OBESITY IN KIDNEY TRANSPLANTATION: A PROSPECTIVE COHORT STUDY FROM FRENCH REGISTRIES BETWEEN 2008 AND 2014.

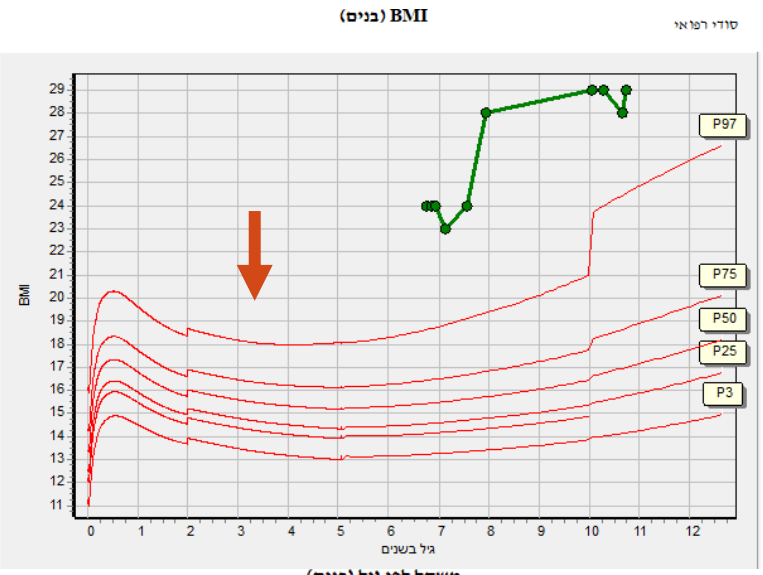
- Greater risk in obese patients of delayed graft function (24.6 versus 12.3%, $P < 0.001$),
- Cardiovascular complications
- Post-transplant diabetes
- Post-transplant length of hospital stay was also significantly longer in obese patients

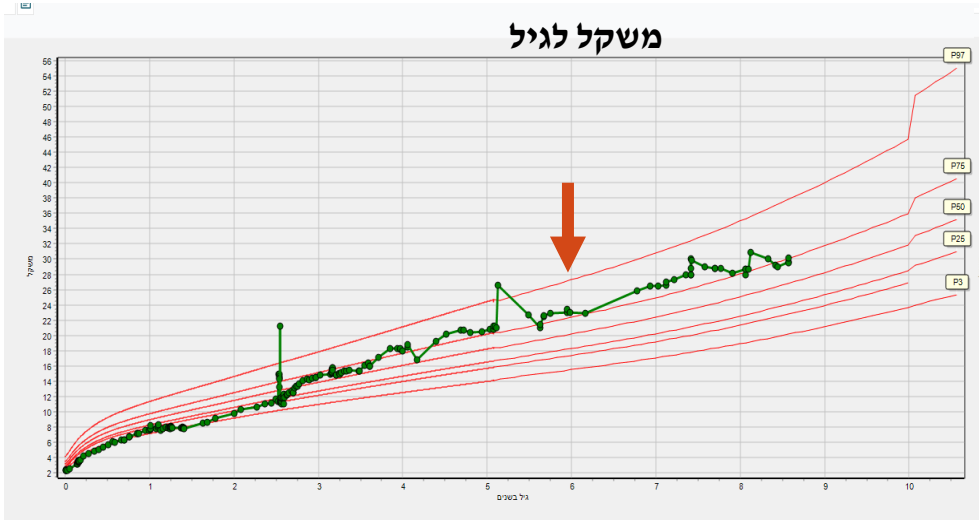
- Mean BMI at transplant was 29.1 kg/m2 in obese WL and 32.4 kg/m2 in obese nWL ($P < 0.001$).
- Dialysis duration was longer in the obese WL than in the obese nWL and the time between start of dialysis and registration on the waiting list was longer for obese WL
- Graft survival at 5 years was significantly lower in obese WL than in obese nWL
- In contrast, patient survival at 5 years was comparable in the two groups
- Graft survival was significantly lower in obese WL than in obese nWL, whereas patient survival was similar in the two groups

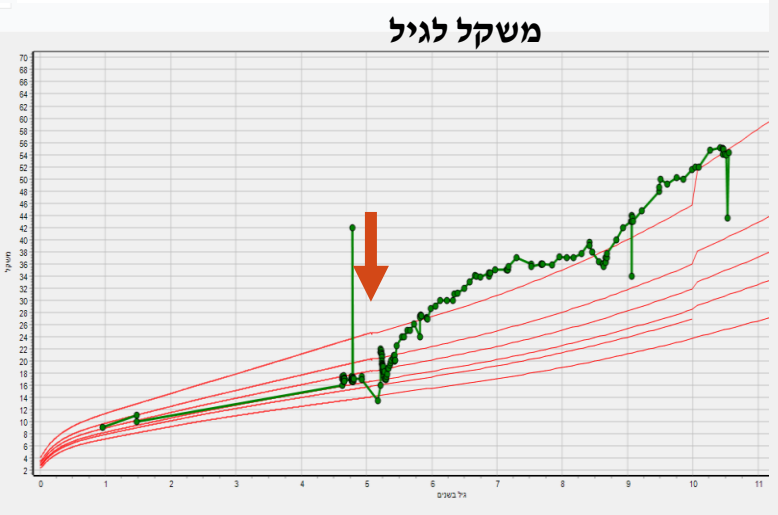
OUR EXPERIENCE

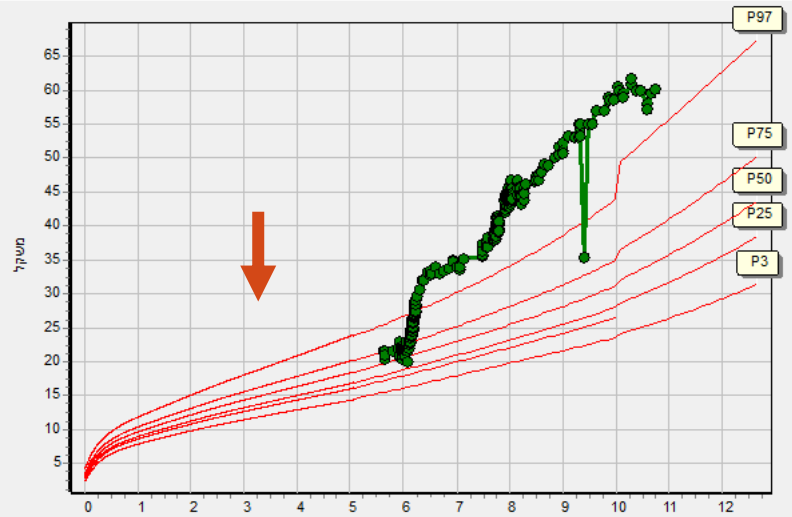






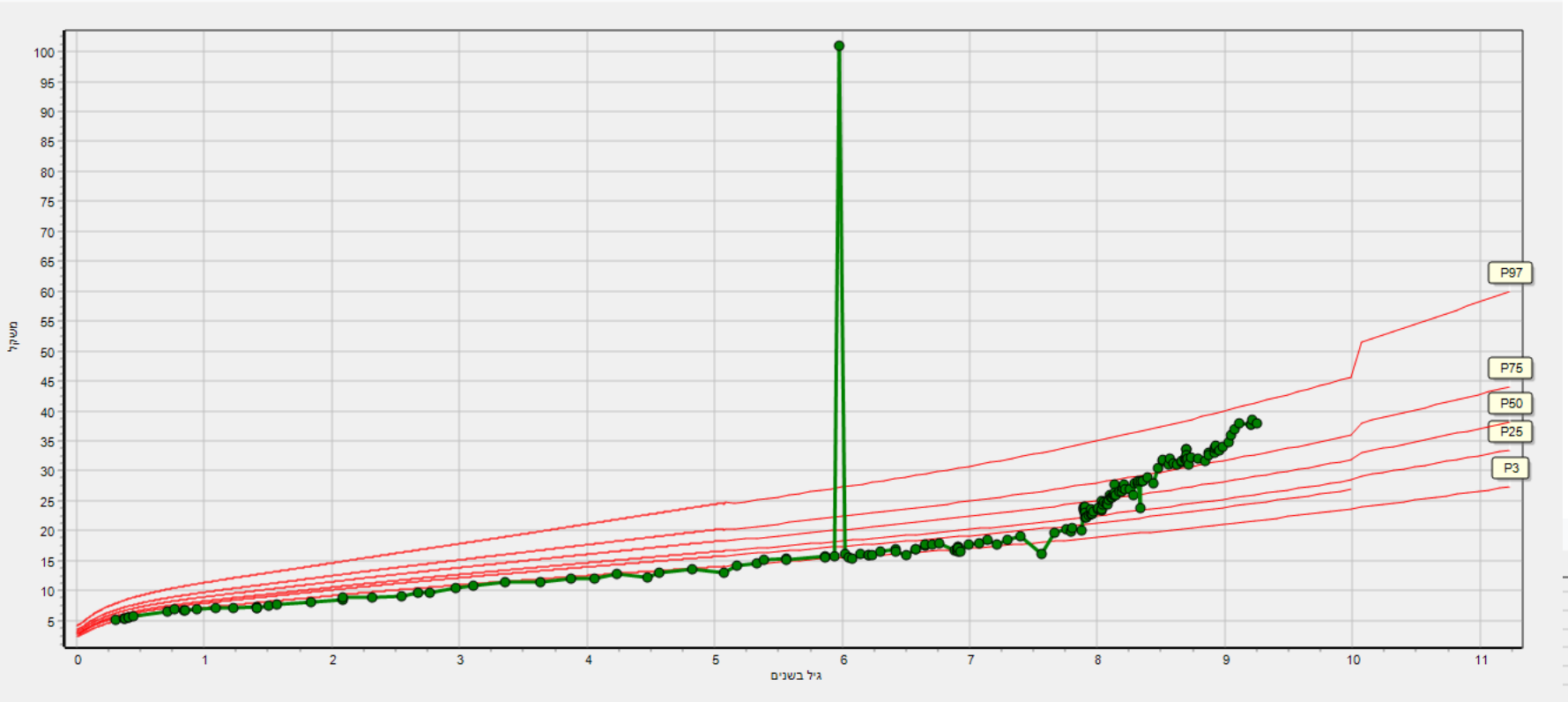


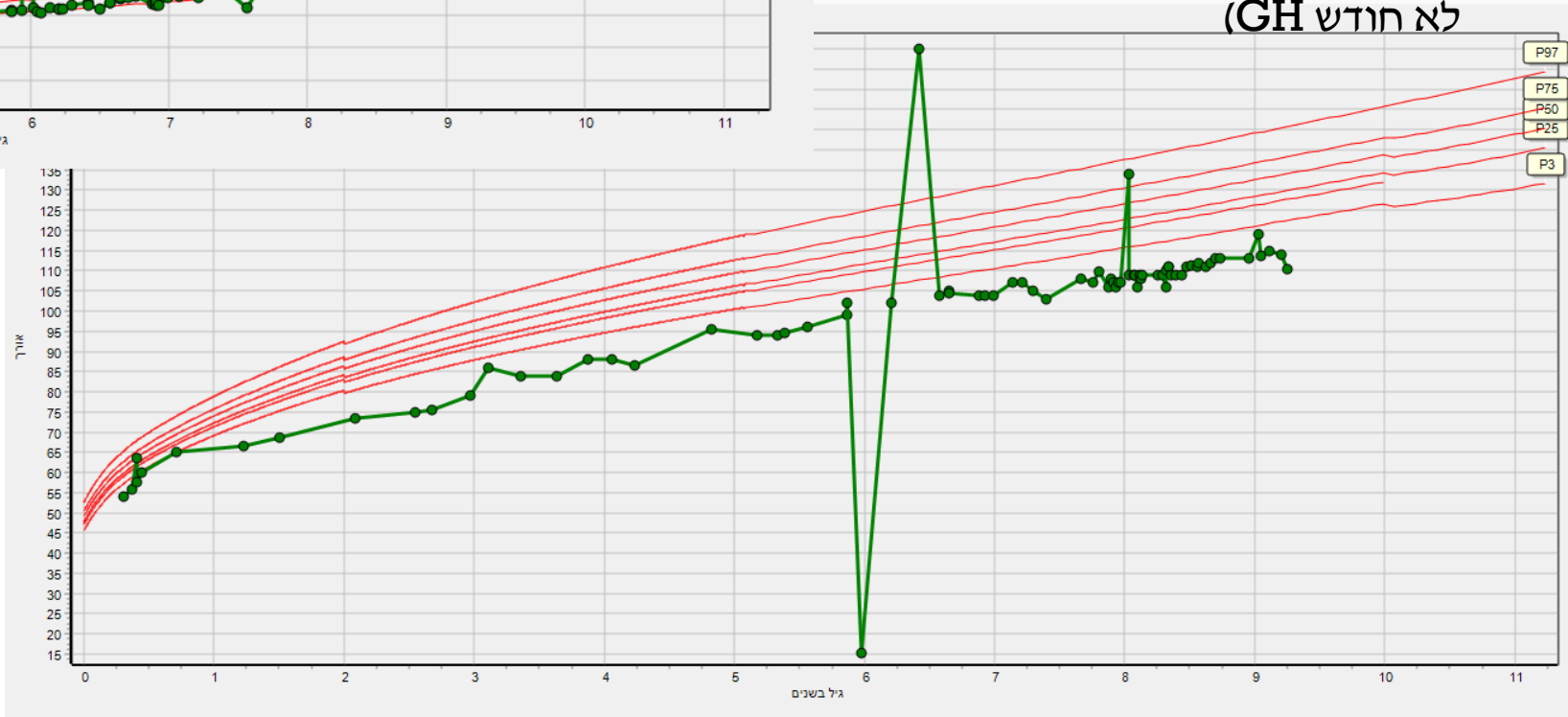




ע.ג'.

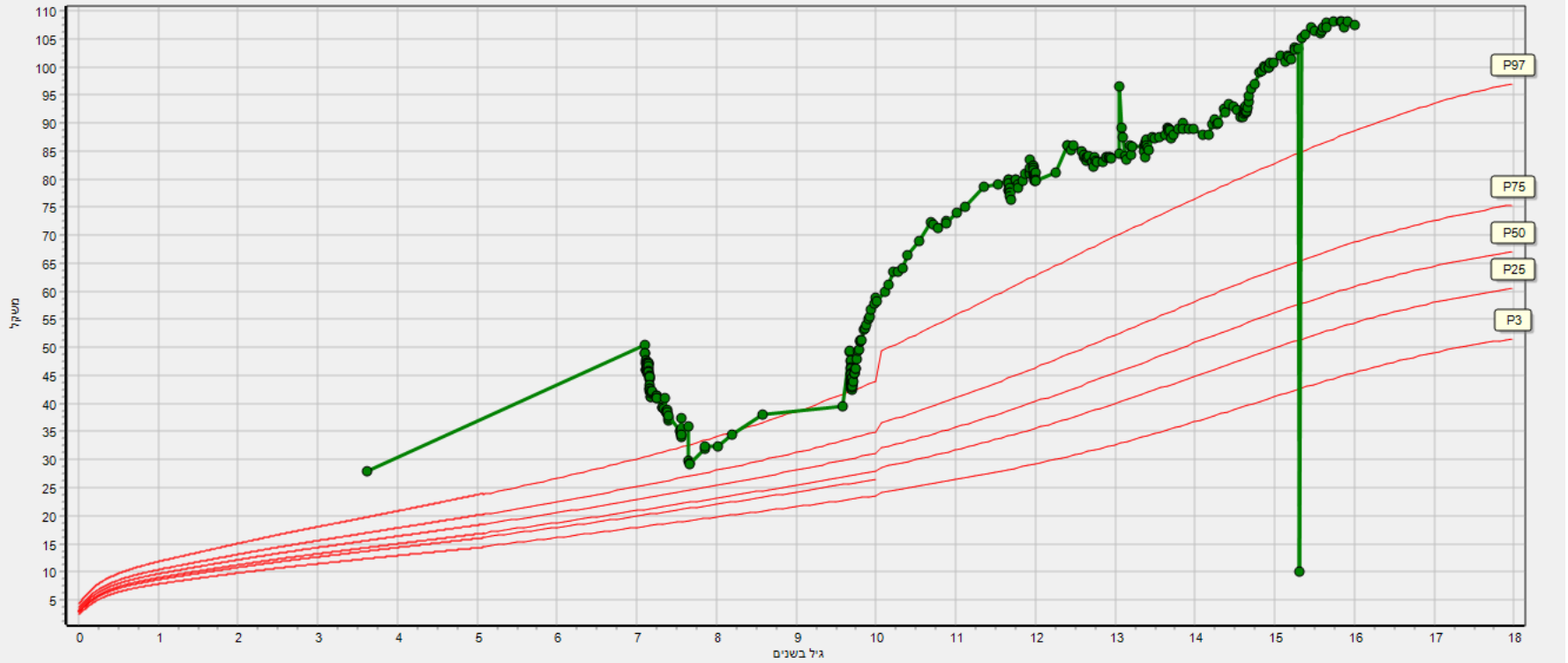
איס"ק כליות מגיל 6 חודשים על רקע כליות דיספלסטיות (בירור גנטי לא אבחנתי)
השתלה 10.10.23 מהמת
ללא ארועי דחיה
BK נפרופטיה
Pseudotumor cerebri (לכן לא חודש GH)

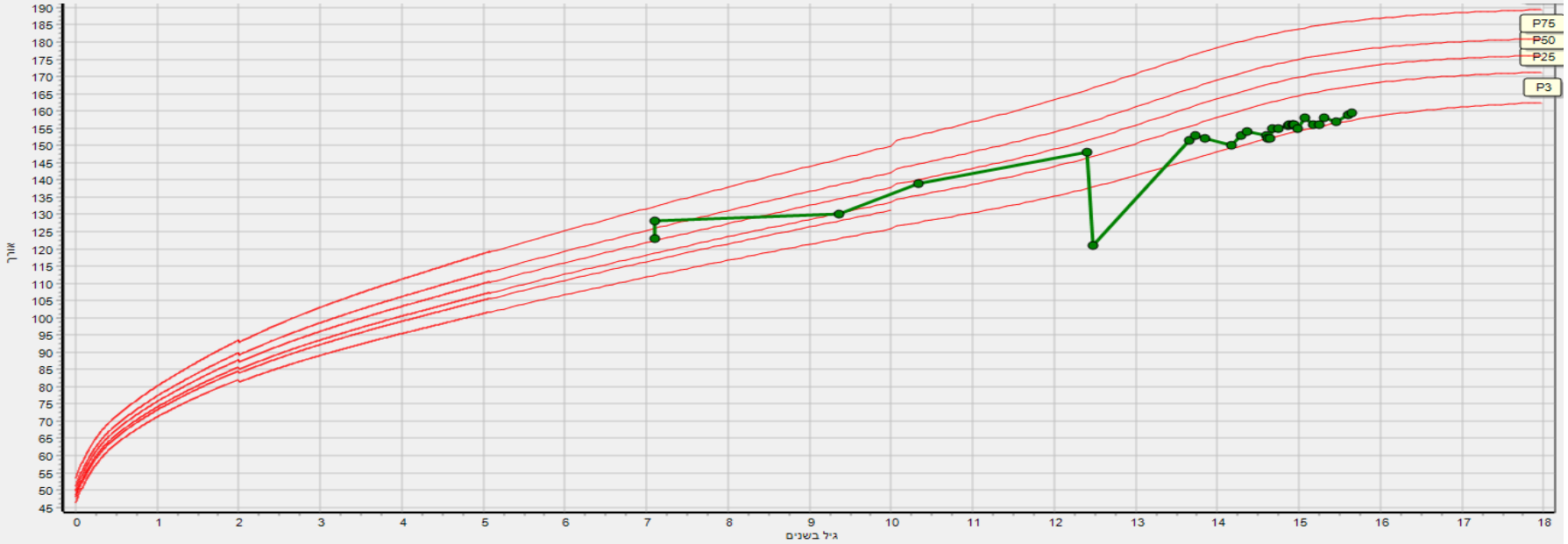




ח.ע.

- תסמונת נפרוטית עמידה לטיפול
- השתלה מהמת 28.9.18 (גיל 11)
- הישנות FSGS מספר פעמים
- דחיה הומורלית כרונית
- סכרת מטופלת בglucophage
- תי"ל ל- GLP1R agonists





OUR EXPERIENCE

- 2019-2024 33 pediatric renal transplantation
- 3/33 (10%) obese prior to transplantation
- 9/33 (27%) obesity and severe obesity post-transplantation
- 2/9 (1/3 prior to transplantation) history of immunologic disease and steroid treatment in the past
- Anti rejection protocol in all pediatric transplanted patients in our center include steroids, tacrolimus, MMF
- 1/9 (11%) was treated with high dose steroids post-transplantation due to rejection episode

TREATMENTS FOR OBESITY

- מרפאת אורח חיים בריא – דיאטנית, רופא ספורט, קרדיולוג
- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) (ozempic, liraglutide)
- Side effects – GIT symptoms, acute pancreatitis,
- sGLT-2 inhibitors –
- S/e recurrent uti, AKI, hypotension
- Setmelanotide in central hyperphagia –
- S/e hypokalemia??? Dehydration and AKI

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Efficacy and safety of setmelanotide, a melanocortin-4 receptor agonist, in patients with Bardet-Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial with an open-label period

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CONTRIBUTORS

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SUMMARY

- Weight gain, over-weight and obesity are prevalent in the pediatric population and increasing prevalence in the pediatric kidney transplant population than in the past decades
- Rapid weight gain and obesity have been shown to effect outcomes of kidney transplant and long-term cardiovascular risk, which is already increased in the pediatric CKD population
- There are conflicting results regarding the effect of weight loss prior to transplantation and scares literature regarding the effect of post-transplant weight loss

EFFECTIVE WEIGHT LOSS INTERVENTIONS

- **Lifestyle and Behavioral Modifications**: The Kidney Disease Outcomes Quality Initiative (KDOQI) recommends therapeutic lifestyle measures, including dietary changes and increased physical activity, as first-line interventions.
- **Nutritional Counseling**: Regular dietary assessment and counseling.
- **Pharmacologic Interventions**: like glucagon-like peptide-1 receptor agonists (GLP-1RAs)
- **Bariatric Surgery???**