Obesity Related Hypertension

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האיגוד הישראלי לנפרולוגית ילדים
ISPN The Israeli Society of Pediatric Nephrology

קווים משיקים ברפואת הילדים

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האגוד הישראלי לאנדוקרינולוגיה פדיאטרית

Introduction

1 Definition

Obesity: BMI ≥95th percentile for age/sex

Hypertension: BP ≥95th percentile for age/sex/height

2 Rising Prevalence

Sedentary lifestyles, poor diet, increased screen time.

COVID-19 pandemic accelerated the trend

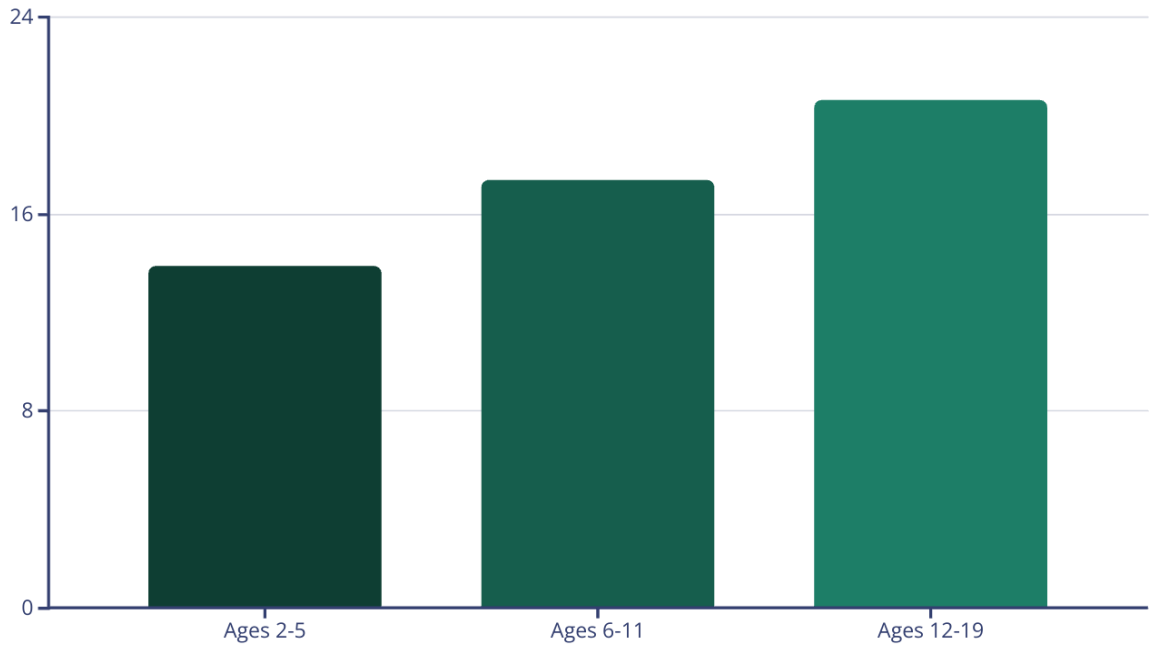
3 Health Impact

Increased risk of cardiovascular and metabolic disorders in youth

Epidemiology of Obesity & Hypertension in Youth

- **Hypertension in Overweight & Obese Youth**
  - **Primary hypertension** is the most common form in adolescents
  - Prevalence ranges from **5% to 30%**, increasing with **higher BMI percentiles**.
  - Obesity is the strongest risk factor for hypertension (HTN) in childhood
  - Children with obesity often exhibit abnormal diurnal BP variation
  - High prevalence of Masked Hypertensiom

- **Prevalence of Pediatric and Adolescent Obesity NHANES data (2011-2014)**:



Pathophysiology How obesity leads to hypertension

SNS Activation

Leptin Overstimulation

Fat cells release leptin, overstimulating the brain

Increased Heart Rate

SNS activation leads to higher heart rate and vasoconstriction

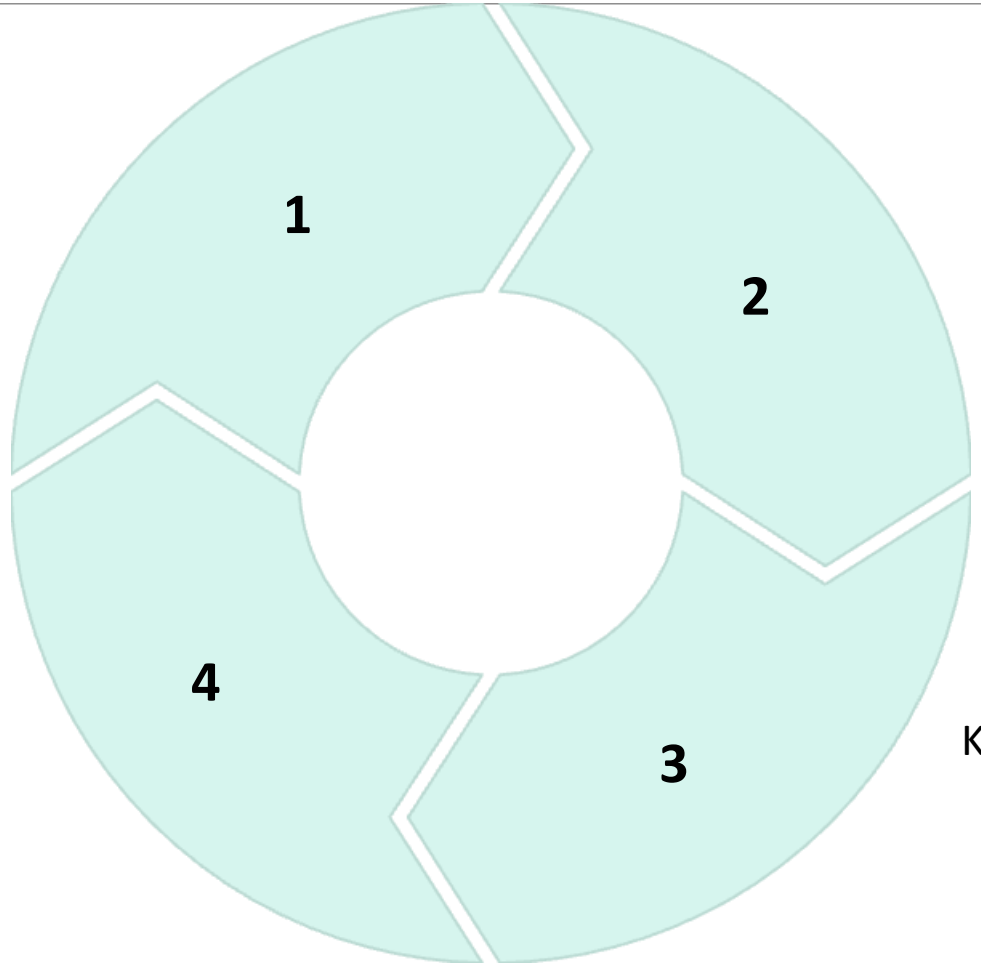
Chronic Elevation

Prolonged SNS activation results in higher blood pressure

RAAS Activation

Fat Cell Release

Adipose tissue releases renin and angiotensin II



Vasoconstriction

Angiotensin II causes blood vessel narrowing

Sodium Retention

Kidneys retain more sodium, increasing blood volume

Increased BP

Higher blood volume and vasoconstriction raise blood pressure

Inflammation & Endothelial Dysfunction

- Obesity-Related Inflammatory Response:
  - Visceral fat acts as an endocrine organ, releasing pro-inflammatory mediators (IL-6, TNF-α, MCP-1) that impair endothelial function
  - Reduced nitric oxide (NO) → Impaired vasodilation → Stiff, narrow blood vessels
  - Chronic inflammation contributes to vascular stiffness, atherosclerosis, and increased BP

Higher systemic inflammation in obese children is associated with early vascular damage and hypertension progression.

Insulin Resistance, Adipokines & Sodium Retention

- **Leptin is produced by adipose tissue, and its levels increase proportionally to adipose mass**
- **Leptin stimulates the (SNS) to increase thermogenesis and energy expenditure**
- **Increased sodium retention in the kidneys → Higher blood volume and BP**
- **<u>Adiponectin & Hypertension Risk in Obese Children</u>**
- **Adiponectin levels are reduced in obesity due to lower tissue insulin sensitivity**
- **Lower adiponectin contributes to endothelial dysfunction, increasing the risk of hypertension and vascular damage**
- **A prospective study in Ningxia (1184 children with obesity) found:**
- **Higher leptin & lower adiponectin levels in obese children compared to normal-weight peers**

Uric acid, Obesity and HTN

- **Serum UA levels have been shown to correlate and predict the development of HTN**
- **Risk factors associated with hyperuricemia include obesity, diabetes, metabolic syndrome**

Proposed mechanism

- **Promotes oxidative stress and endothelial dysfunction**
- **Reduces nitric oxide, causing blood vessel constriction**
- **Increases sodium retention and inflammation**

- **Some Studies show benefits of uric acid-lowering drugs in adolescents**

Risk Factors

Severe Obesity

BMI ≥120% of the 95th percentile

Early Onset

Early obesity onset worsens long-term risks

Genetics

Family history plays a role

Unhealthy Diet

High-calorie, high-sodium foods increase risk

Other factors include physical inactivity excessive screen time, and sleep deprivation

Clinical Presentation & Diagnosis

- **Often Asymptomatic**
- **Severe Cases**: Headaches, dizziness, vision issues
- **BP Measurement**: Correct cuff size, multiple readings
- **Ambulatory BP Monitoring (ABPM)** for accuracy
- **Lab Tests**: Lipid profile, fasting glucose, kidney function

Abnormal BP Patterns in Obese Children

- Reduced nocturnal BP dip increases

end-organ damage risk.

- Masked Hypertension (MH):
  - Valent Morić et al. found MH prevalence was 31.6% in obese children, vs. 5.7% in non-obese children.
- **<u>AAP recommends screening for HTN in obese children at every clinic visit starting at age 3.</u>**

Complications of Uncontrolled Hypertension

- **Cardiovascular Disease**: Early atherosclerosis, heart failure
- **Left Ventricular Mass (LVM) Increase** → Risk of **heart failure**
- **Carotid Intima-Media Thickness (cIMT)** → Early **atherosclerosis**
- **Chronic Kidney Disease (CKD)**
- **Cognitive & Psychological Issues**: ADHD, depression

Management

Lifestyle Changes

- **Weight Loss**: 5-10% reduction **lowers BP**
- **DASH Diet**: Low sodium, high potassium, less processed food
- **Physical Activity**: ≥1 hour/day of aerobic & strength training
- **Screen Time**: Less than 2 hours/day

Medications

- **ACE Inhibitors** (lisinopril, enalapril) – Kidney protective
- **ARBs** (losartan) – Alternative for ACE inhibitor intolerance
- **Calcium Channel Blockers** (amlodipine) – Vasodilation
- **Diuretics** – Fluid retention control

GLP1 RA

- *Safety and Efficacy of Glucagon-Like Peptide-1 Receptor Agonists in Children and Adolescents with Obesity: A Meta-Analysis." The Journal of pediatrics (2021*)
- A Meta-Analysis of Nine studies involving 574 participants
- Mean age across all included participants was 14.15 years
- 3 involved exenatide and 6 involved liraglutide.
- **GLP-1 receptor agonists use caused a modest decrease in systolic blood pressure**

  (MD -2.30 [-4.11,-0.49] mm Hg)

Glucagon-like peptide-1 receptor agonists modestly reduced blood pressure among patients with and without diabetes mellitus: A meta-analysis and meta-regression

Search Strategy

PubMed/MEDLINE
Ovid/Embase
ClinicalTrials.gov
(*n* = 4178)

RCTs with GLP-1RA vs Placebo (*n* = 63)

Primary Endpoint: mean difference in SBP & DBP

Subgroup analyses:

- duration of treatment
- dose
- mode of administration
- mean baseline SBP
- DM status

DBP (GLP-1RA vs. Placebo)		
GLP-1RA	MD (mmHg)	95% CI
Exenatide	−0.94*	(−1.78, −0.1)

Demographics

(*n* = 53 072)

Gender

20 959 (39.49%)

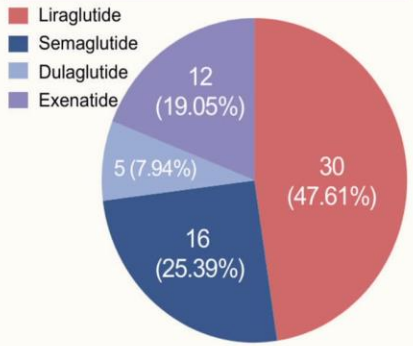
32 113 (60.51%)

DM Status

22 083 (41.69%) with DM

30 888 (58.31%) no DM

Type of GLP-1RA



Outcome: Patients on GLP-1RA experienced significant SBP lowering compared to placebo, independent of its effect on glycemic control. DBP reduction was only significant in the exenatide group

benefit increased with >24 weeks treatment

SBP (GLP-1RA vs. Placebo)		
GLP-1RA	MD (mmHg)	95% CI
Semaglutide	−3.40*	(−4.22, −2.59)
Liraglutide	−2.61*	(−3.48, −1.74)
Dulaglutide	−1.46*	(−2.20, −0.72)
Exenatide	−3.36*	(−3.63, −3.10)

Effects of GLP1 receptor agonists on blood pressure in overweight or obese patients - a meta-analysis of randomized controlled trials

1 BACKGROUND

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are efficacious in diabetes mellitus and weight loss

However, the effects of GLP-1 RAs on *blood pressure* (BP) in overweight or obese patients is unknown

2 SYSTEMATIC SEARCH AND METHODOLOGY

MEDLINE, EMBASE, CENTRAL searched
5254 records screened

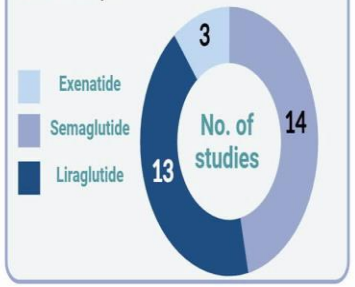
Inclusion Criteria

- OBESE OR OVERWEIGHT PATIENTS
- GLP-1 RA ORAL OR SUBCUTANEOUS
- OUTCOME: CHANGE IN SBP/ DBP
- RANDOMIZED CONTROLLED TRIALS

3 POPULATION

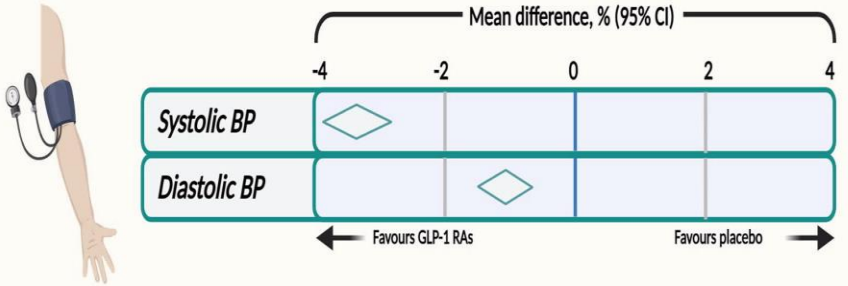
30 randomized controlled trials included

37072 patients in total



4 RESULTS

GLP-1 RAs demonstrated **mean BP reduction** in overweight or obese patients of...



...consistent across diabetic status, formulation, mode of administration, treatment duration, and was *not influenced* by baseline characteristics,

CONCLUSION

GLP-1 RAs demonstrate *significant SBP and DBP reduction* in overweight and obese patients, consistent across diabetic status, mode of administration and treatment duration

SBP and DBP reduction was *not influenced by baseline characteristics* such as age, gender, HbA1c, BMI and diagnosed hypertension

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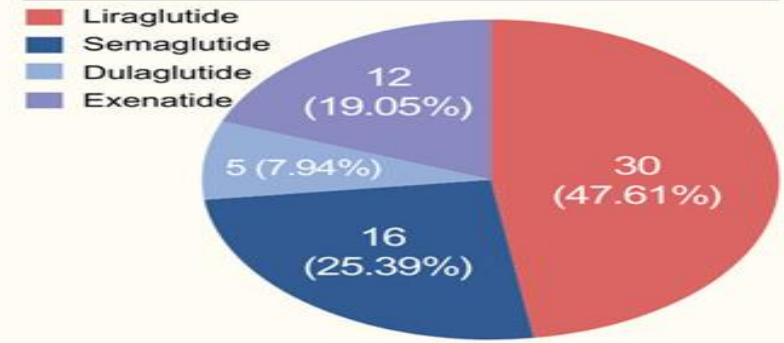

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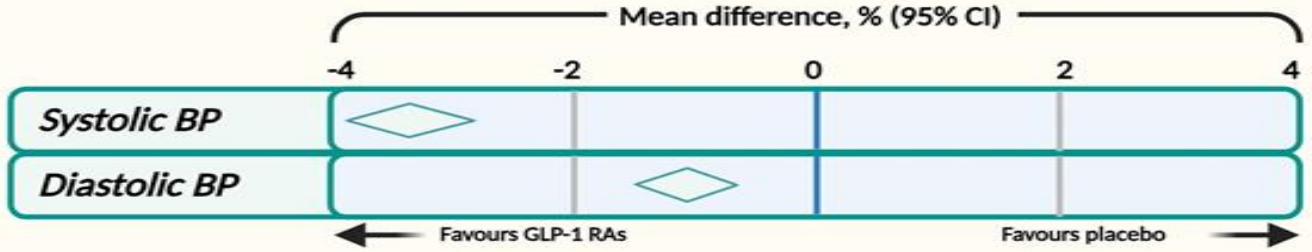

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Bariatric Surgery

Teen-LABS Study

1 Study Overview

Teen-LABS study analyzed 242 adolescents undergoing bariatric surgery.

Procedures included RYGB, VSG, and AGB.

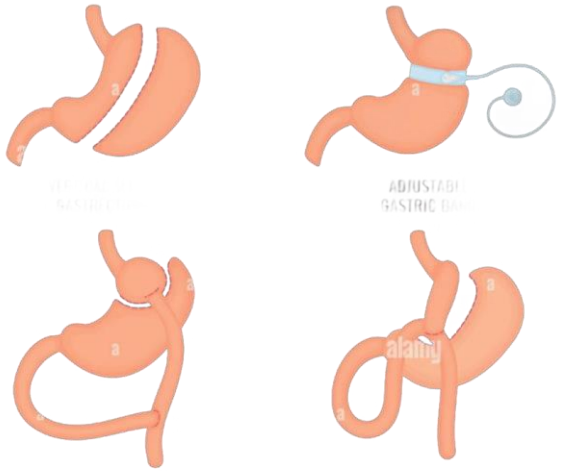
2 Blood Pressure Reduction

Systolic BP decreased from 125.6 to 118.2 mmHg.

Diastolic BP decreased from 74.4 to 71.7 mmHg.

3 Normalization of BP

44% had elevated BP before surgery → Dropped to 15% at 3 years



Bariatric Surgery in Adults

- *The Impact of Bariatric Surgery Versus Non-Surgical Treatment on Blood Pressure: Systematic Review and Meta-Analysis Obesity Surgery (2021) 31:4970–4984*

Impact of Bariatric Surgery on Blood Pressure Reduction - 19 RCT 1353 patients

- **Systolic Blood Pressure (SBP) Reduction**:
  - **Mean reduction of -3.94 mmHg** (CI: -6.00 to -1.87, $p < 0.001$).
- **Diastolic Blood Pressure (DBP) Reduction**:
  - **Mean reduction of -2.69 mmHg** (CI: -3.99 to -1.39, $p < 0.001$).
- **Long-Term Effectiveness**:
  - Sustained BP-lowering effect for up to **5 years post-surgery**
  - Reduced need for **antihypertensive medications**

Conclusion

- **Obesity-related hypertension in children and adolescents is a growing public health concern.**
- **Early identification and intervention** are crucial to preventing long-term complications.
- **Lifestyle modifications**, including weight loss, a balanced diet, and regular physical activity, are the **first-line approach** in management.
- **Pharmacological treatment** is needed for **severe or resistant hypertension**.
- **Bariatric surgery** offers **significant benefits** in reducing blood pressure in adolescents with severe obesity.
- **Routine hypertension screening** should be incorporated into pediatric care as recommended by the **AAP.**