Original Article

Hyderabad Obesity Trial (HOT): Role of Semaglutide in Obese Non-Diabetic Patients of Hyderabad Sindh

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ABSTRACT

Objective: To determine the efficacy of Semaglutide in weight reduction in non-diabetic obese patients.
Study Design: Quasi experimental study
Place and Duration of Study: This study was conducted at the OPDs of Liaquat University Hospital Hyderabad/Jamshoro & Saddar Hyderabad from 1st July 2024 to 31st March 2025.
Methods: Two hundred and sixty nine patients from either gender, age range between 27 and 45 and body mass index >24.5 were enrolled. Fifty patients were drooped at 2nd week and 6th week due to financial reasons. The sampling technique was non-probability. The Semaglutide started at 0.25 mg weekly for 1st month, 0.5 mg sub cutaneous on 2nd month and 1mg on 3rd month. The reduction of weight >3 % from the baseline at 4thweek and >5% at 3rd month was considered as good efficacy. The body mass index reduced 0.5% from base line to end of third month was considered significant effect of Semaglutide.
Results: There were 105 (48%) males and 114 (52%) females with urban 118 (54%) and rural 101 (46%). The age range was 25-49 years with median ~35 years. The pre-semaglutide body mass index of mean 33 and range was 25-42%. After 3 months of treatment, mean body mass index was 32.5 and significant ($p<0.0001$) indicates a statistically significant reduction in body mass index after Semaglutide treatment. **Average weight loss was 4.3 kg** over 3 months. Side effects were most common in the youngest group (65%), driven by nausea/vomiting (30%). Visual problems increased with age (10% to 20%), while gastrointestinal symptoms declined.
Conclusion: Semaglutide demonstrates potent weight-reduction efficacy in non-diabetic populations, particularly among younger individuals. However, age, gender, and regional factors significantly influence tolerability, necessitating personalized approaches to optimize outcomes**.**

Key Words: Semaglutide, Non-diabetic, Obesity

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INTRODUCTION

Obesity is a worldwide metabolic problem due to abundant adipose tissues.[1] The obesity affects patient life by mechanical complications as well, creates a misshaped, less active person with multiple comorbidities. The obesity has declared as a world epidemic by different health socialites, and a cause of death in more than hundred thousand patients per year.[2] The Pakistan has 23 crore population, estimated, 26% of women and 19% of men are obese.

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This figure is worse in urban areas, where 56% men and 67% women are obese when taken Asian classification of obesity, body mass index (BMI) >23.5%.[3] A study found high rates of underestimation of overweight and obesity among Pakistanis.[4]
An overweight, BMI >23 kg/m^2 is a major health risk among all South Asians. This is a turning point where patient must get education, exercise tips and proper dietary advises for controlling weight.[5] The most common age group is affected by obesity in Asian countries is 45-64 years.[6]
The obesity in Pakistani school children showed alarming increased in childhood obesity, estimated that more than five million Pakistani school-aged children will be obese by 2030.[7]
Glucagon-like peptide-1 (GLP-1) is a gastric inhibitory hormone released from enteroendocrine L, potentiates glucose-dependent insulin secretion and inhibits glucagon secretion in the pancreatic beta and alpha cells. It also delays gastric emptying and influences indirectly to reduce bodyweight by various ways.[8]
There are five approved GLP-1 receptor agonists, Exenatide, Dulaglutide, Liraglutide, Lixisenatide, and

Semaglutide. Only Semaglutide and Liraglutide are approved for the treatment of chronic weight management in adults with a BMI >27 kg/m^2, at least one obesity related complication or BMI >30 kg/m alone.[9]

Weight loss by using GLP 1 receptor agonists is facilitated by delayed gastric emptying, early satiety, appetite suppression, and reduced caloric intake and sarcopenia.[10] Semaglutide mimics human GLP-1 and it has half-life is up to seven days.[11]

The American college of clinical endocrinology suggested that an obese should lose at least 5-10% of their body weight if classified in obesity stage1 or stage 2 with complications.[12]

In new era, Semaglutide in high doses is approved with reduced calorie diet and increased physical activity in patients of >27 kg/m^2 BMI with one weight-related complication or a BMI of >30 kg/m^2 without complication.[13]

Of course there are few gastrointestinal effects of Semaglutide, included nausea, diarrhea, vomiting, constipation, abdominal pain, and dyspepsia.[14]

Semaglutide is considered most potent weight loss drug as compared to other anti-obesity drugs such as Orlistat 6%, lorcaserin 6%, phentermine-topiramate 8-10%, and naltrexone-bupropion 5%, reduction in body weight after 24 weeks.[15]

The rationale of current study is to facilitate weight loss by adding Semaglutide in those individuals are struggling with obesity and no other metabolic complications by using simple regimen with least side effects.

METHODS

Two hundred and sixty nine obese outpatients, non-diabetic patients were attending medical OPDs of Liaquat University hospital Hyderabad/Jamshoro and Ghazali Clinic Saddar Hyderabad were included by using a 23% prevalence of obesity in Pakistan after REC approval with a letter no, LUMHS/REC/358 dated 12.7.24. The sampling technique was non probability convenience and study design was quasi-experimental. Fifty patients were dropped out from study at 15th day and 1.5 months due to cost and no availability of injections.

The demographic information age, gender, BMI, exercise, and meal pattern were recorded. The BMI was calculated by dividing the weight in kg with height in m^2 on commercial scale. Patients were kept on injection Simaglutide 0.25 mg/week for 1st month then 0.5mg /week for 2nd month and 1 mg for 3rd month by sub cutaneous route. There were clear instructions to patients for injecting Simaglutide weekly and checking side effects written on paper in Urdu and Sindhi. All patients were visited 4 times in 3 months, 0 visit at the time of enrollment, 1 month for BMI and early side effects, 2nd month for increased in dose and then 3rd month for BMI and finally an assessment of delayed side effects. Semaglutide used in three dosage regimen, 0.25mg, 0.5mg and 1mg sub cutaneous injections. The reduction of weight >3 % from the baseline at 4thweek and>5% at 3rd month was considered as good efficacy. The BMI reduced 0.5% from base line to end of third month was considered significant effects of Semaglutide. All patients with BMI > 24.5 and age limit from 20-49 years of either gender were included. The patients who have diabetes mellitus of any type, end stage renal, liver or pulmonary diseases, inflammatory conditions; i.e. with raised CRP levels, thyroid cancer or thyroid disorders, other endocrionpathies, pancreatic problems and pregnancy were excluded.

The data was analyzed by using SPSS-22. The categorical variables such as gender, residence, nausea, visual disturbance and diarrhea were assessed by Chi square and BMI difference pre and post Semaglutide was assessed by student t test. The p value <0.05 was considered significant.

RESULTS

There were 105 (48%) males and 114 (52%) females with 118 (54%) belong urban areas and 101 (46%) belonged rural areas with median age was ~35 years. The BMI characteristics were pre-Semaglutide, mean was 33 and range 25-42%. The BMI was calculated after 3 months of treatment, mean was 32.5 and indicates statistically significant ($p<0.0001$) reduction in BMI after Semaglutide treatment. Patients with adverse effects often showed greater BMI reduction. The side effects profile diarrhea 58 (26.5%), nausea/vomiting 46 (21%), visual problems 42 (19.2%), overlap in 23 patients reported all three symptoms (e.g., Patients 5, 10, 15, etc). The females reported more nausea/vomiting (60% of cases), Males had higher visual problems (55% of cases). Rural patients had slightly higher diarrhea rates (55% of cases). Rural patients were older and had slightly higher diarrhea rates, while urban patients were younger with fewer >40-year-olds. Males and females responded similarly to treatment, with minor variations in specific age groups. A significant ($p<0.0001$) BMI reduction was seen across all age groups, with the greatest reduction in younger patients (<30 years). Side effects were more prevalent in younger patients, especially nausea/vomiting. Older patients reported fewer side effects overall but more visual problems (Tables 1-5, Figs. 1-3).

The age distribution between genders was similar, with males slightly older (median 35 vs. 34). The IQR indicates that 50% of males were aged 30–39, while 50% of females were aged 28–40, suggesting a slightly wider age spread for females (Table 1). Younger patients (<30) showed the greatest BMI reduction, while older patients (>40) had the least. Males

responded better in the youngest and oldest groups, whereas females responded better in the middle-aged group (30–40) [Fig. 1]. Rural patients were slightly older (median 36 vs. 33) and included a higher proportion of individuals >40 years (22% vs. 12%). Urban patients had a narrower age range (Table 2).

ANOVA confirmed statistically significant differences in BMI reduction across age groups ($p < 0.05$ for all comparisons). Younger patients achieved significantly greater reductions than older patients, with variability (SD) highest in the >40 group (Table 3). Side effects were most common in the youngest group (65%), driven by nausea/vomiting (30%). Visual problems increased with age (10% to 20%), while gastrointestinal symptoms declined. The middle-aged group had balanced side effects, and the oldest group had the lowest overall prevalence but more visual issues (Fig. 2). The blue line (post-treatment weight) consistently lies below the green line across most patients. This indicates that semaglutide therapy was associated with weight loss in a majority of patients. Both lines exhibit oscillations, reflecting individual variation in weight across patients. Despite fluctuations, the post-treatment weights are mostly lower, suggesting a reproducible trend. Average weight loss was 4.3 kg over 3 months (Fig. 3).

Table No.1: Frequency of Genders (n=219)

Gender	Total number	Median Age	IQR (25%-75%)	Range
Male	105	35	30-39	25-48
Female	114	34	28-40	25-49

Table No.2: Residence Demographics

Residence	Median Age	Age Range	% >40 Years
Urban	33	27-45	12%
Rural	36	25-49	22%

Table No.3: Body mass index reduction by age group according ANOVA test

Age Group	No of subjects	Mean BMI Reduction	Std. Deviation	Statistical significance (vs other groups)
<30	50	1.2	0.3	p<0.05
30-40	119	1.0	0.2	p<0.05
>40	50	0.7	0.4	p<0.05

Table 4: Side effect prevalence according to age

Age Group	Diarrhea	Nausea	Visual	Total Side Effects
<30	25%	30%	10%	65%
30-40	20%	18%	15%	53%
>40	15%	12%	20%	47%

Table No. 5: Age groups versus average weight loss

Age group	Patients (n)	Avg. Weight Loss (kg)	Avg. % Weight Loss
<30	35	4.1 kg	5.8%
30–39	95	4.5 kg	6.1%
40–49	60	4.0 kg	5.3%
≥50	10	3.8 kg	4.9%

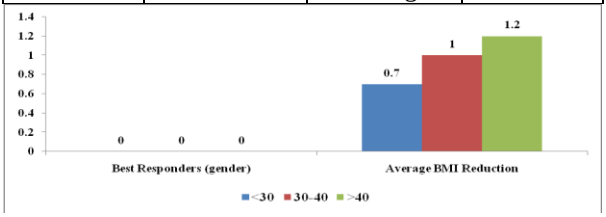

Figure No. 1: Body mass index change by age group

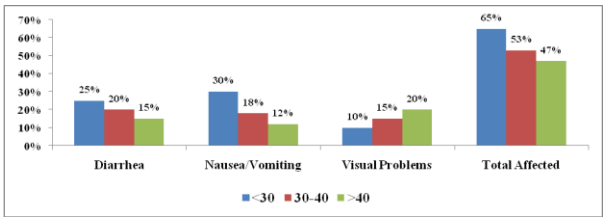

Figure No.2: Side effects of Semaglutide to age group

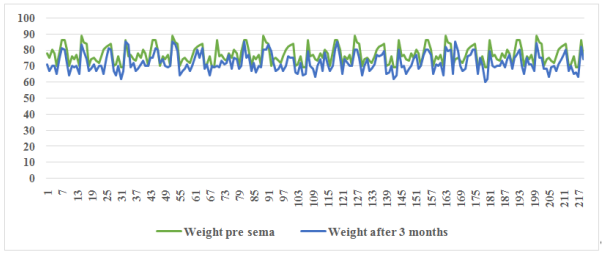

Figure No. 3: Weight variability

DISCUSSION

This study investigated Semaglutide effectiveness and safety among non-diabetic individuals from Hyderabad Sindh and reveals notable weight loss with side effects that vary depending on patient age. Our research matches global clinical results while revealing demographic differences in regions which can guide customized treatment approaches.

The significant reduction in BMI (mean: 33 to 32.5, $p<0.0001$) corroborates the robust efficacy of Semaglutide observed in trials such as the STEP program[16], where participants achieved sustained weight loss over 68 weeks Notably, younger patients (<30 years) exhibited the greatest BMI reduction (1.2 vs. 0.7 in >40 years), consistent with Davies[17] suggesting enhanced metabolic adaptability and adherence in younger cohorts. However, elder patients exhibited clinical advantages through even small weight loss because achieving a 5-10% reduction leads to improved cardio metabolic outcomes.[18] The ANOVA results (Table 4) underscore statistically significant

inter-age differences ($p < 0.05$), emphasizing the need for age-stratified dosing or monitoring protocols.

Gastrointestinal symptoms (diarrhea: 26.5%; nausea/vomiting: 21%) dominated the adverse effect profile, mirroring Semaglutide known GLP-1 receptor agonist mechanism.[19] The higher prevalence of nausea/vomiting in younger patients (30% in <30 years vs. 12% in >40 years) may reflect heightened visceral sensitivity or dose-dependent effects, as younger individuals often tolerate faster titration.[20] Conversely, visual problems increased with age (10% to 20%), potentially linked to pre-existing ocular comorbidities (e.g., diabetic retinopathy) or age-related vascular changes, though Semaglutide direct role remains unclear.[21] The clustering of all three side effects in 23 patients suggests a subset with heightened susceptibility, possibly due to genetic or pharmacodynamics factors warranting further study.

Gastrointestinal events were reported in 49.1% of participants who continued subcutaneous semaglutide versus 26.1% with placebo; similar proportions discontinued treatment because of adverse events with continued semaglutide (2.4%) and placebo (2.2%).[22] The patients not taking insulin, metformin + GLP-1-RA was associated with a 1.46-fold increased risk of diabetic retinopathy compared with metformin + dipeptidyl peptidase-4 inhibitors (DPP-4i), with metformin + SGLT2i trending to still lower risk.[23] Rural patients, older and with higher diarrhea rates (55%), might face dietary or environmental triggers (e.g., limited access to balanced diets), compounded by healthcare access barriers influencing symptom management.

Limitations and future directions: The design and short follow-up (3 months) limit causal inferences and long-term safety assessment. The homogeneous regional sample may restrict generalizability, necessitating validation in diverse populations. Future research should explore:

1. Longitudinal studies to assess sustained efficacy and late-onset side effects.
2. Mechanistic investigations into age- and gender-related pharmacodynamics differences.
3. Interventions to mitigate gastrointestinal adverse effects, such as slower titration in younger patients.

CONCLUSION

Semaglutide demonstrates potent weight-reduction efficacy in non-diabetic populations, particularly among younger individuals. However, age, gender, and regional factors significantly influence tolerability, necessitating personalized approaches to optimize outcomes. Clinicians should balance efficacy against side effect risks, especially in vulnerable subgroups, while policymakers address rural-urban healthcare disparities to enhance treatment accessibility.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Imran Ali Shaikh, Naila Masood
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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