GLP-1 and C-Peptide are associated with Insulin Resistance among PLWH in India

Ivan Marbaniang[1], Shashikala Sangle[1,3], Dileep Kadam[1, 3], Vandana Kulkarni[1], Prasad Deshpande[1], Dhananjay Shere[1], Nikhil Gupte[1,2], Amita Gupta[1,2], Vidya Mave[1,2]

1.Byramjee Jeejeebhoy Government Medical College—Johns Hopkins University Clinical Research Site, Pune, India 2. Johns Hopkins Center for Clinical Global Health Education, Baltimore, Maryland, USA

3. Byramjee Jeejeebhoy Government Medial College, Pune, India

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Background

- Incretins (Glucagon like peptide-1 [GLP-1] and glucose-dependent insulinotropic peptide [GIP]) are important regulators of glucose homeostasis
- Inflammation has been implicated as a cause for insulin resistance (IR) among PLWH
- Little is known about IR among Asian Indians PLWH, even though India has the highest burden of diabetes and the third highest number of PLWH globally
- We aimed to assess the relationship between incretin hormones, inflammatory markers and IR in PLWH

Materials and Methods

- **Database used:** Conveniently sampled, cross-sectional data collected from 350 adult (≥18 years) PLWH
- **Setting:** ART center of BJ Government Medical College & Sassoon General Hospitals Pune, India
- **Period:** September 2015 to August 2016
- **Inclusion criteria:** Non–diabetic adult PLWH on HAART ≥ 1 year
- **Outcome definition:** Insulin Resistance as defined by the Quantitative Insulin Sensitivity Check Index (QUICKI). Individuals with a QUICKI score <0.339 were deemed insulin resistant
- **Assays used:** Bio-Plex Pro™ human diabetes 10-plex immunoassay and 4-plex human cytokine and chemokine assay
- **Analytical techniques:** Logistic regression to identify associations between different components of the assays and insulin resistance

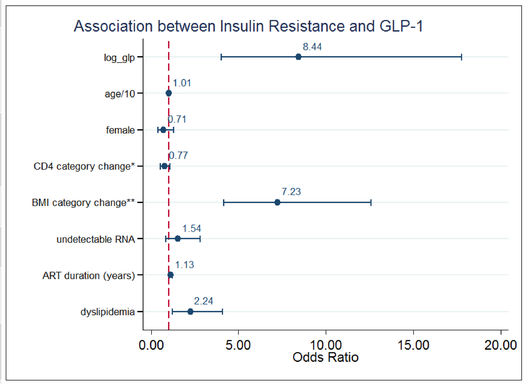
Results

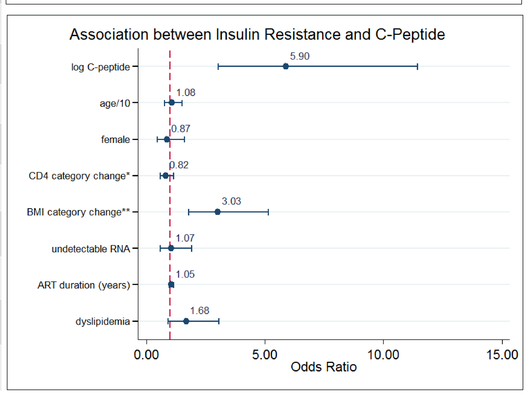
Table 1: Characteristics of the study population

Characteristics	Total n(%)	Insulin resistant n (%)	Insulin sensitive n (%)	p-value
N (%)	**350**	**115 (33)**	**234 (67)**	
Age (years) [Median (IQR)]	40 (35 – 45)	40 (35-46)	40 (35 -45)	0.47
Age groups (years)				
18 – 25	21 (6)	9 (7.8)	12 (5.1)	
25 – 35	65 (18.6)	21 (18.3)	44 (18.8)	0.33
35 – 45	169 (48.4)	49 (42.6)	120 (51.3)	
≥ 45	94 (26.9)	36 (31.3)	58 (24.8)	
Sex				
Male	157 (45)	58 (50)	99 (42)	0.17
Female	192 (55)	57 (50)	135 (58)	
BMI (kg/m2)				
Underweight (<18.5)	100 (29.2)	12 (10.6)	88 (38.4)	<0.05
Normal (18.5 - 24.9)	190 (55.6)	64 (55.6)	126 (55.0)	
Overweight (>24.9)	52 (15.2)	37 (32.7)	15 (6.6)	
Time-updated CD4 (cells/mm^3)				
<350	119 (34.6)	37 (32.2)	82 (35.8)	0.43
350 –500	73 (21.2)	29 (25.2)	44 (19.2)	
>500	152 (44.2)	49 (42.6)	103 (45)	
Undetectable viral RNA (<40 copies/mL)				
Yes	220 (63)	76 (66)	144 (61.5)	0.48
No	129 (37)	39 (34)	90 (38.5)	
Fasting glucose (mg/dL) [Median (IQR)]	88 (83 – 93)	90 (85 – 96)	86 (82– 92)	<0.05
HbA1c (%) [Median (IQR)]	5.1 (4.7 - 5.5)	5.1 (4.6 - 5.5)	5.1 (4.7 - 5.4)	0.52
Hypertension				
Yes	79 (23)	35 (30.4)	44 (19.1)	0.02
No	266 (77)	80 (69.6)	186 (80.9)	
Dyslipidemia*				
Yes	184 (54.6)	74 (68.5)	110 (48.0)	<0.05
No	153 (45.4)	34 (31.5)	119 (52.0)	
Years on HAART [Median (IQR)]	6.2 (3.0 – 8.7)	7.6 (3.6 – 9.1)	5.5 (2.9 – 8.5)	<0.05
GIP (pg/mL) [Median (IQR)]	242 (167 – 372)	316 (199 – 428)	218 (160 – 306)	<0.05
GLP– 1 (ng/mL) [Median (IQR)]	0.3 (0.23 – 0.46)	0.36 (0.26 – 0.57)	0.27 (0.23 – 0.37)	<0.05
C- peptide (ng/mL) [Median (IQR)]	0.7 (0.5 – 1.2)	1.2 (0.9 – 1.6)	0.6 (0.5 – 0.9)	<0.05
Glucagon (pg/mL) [Median (IQR)]	232 (166 – 418)	330 (199 – 562)	218 (155 – 303)	<0.05
Leptin (ng/mL) [Median (IQR)]	2.9 (0.98 – 7.4)	5.0 (2.1 – 11.2)	2.2 (0.8 – 5.9)	<0.05
IL-6 (pg/mL) [Median (IQR)]	2.0 (0.8 – 4.7)	2.0 (0.8 – 4.3)	2.2 (0.8 – 4.9)	0.56
TNF-α (pg/mL) [Median (IQR)]	2.8 (0.9 – 4.6)	2.9 (0.9 – 3.6)	2.8 (0.9 – 5.3)	0.69
IL-10 (pg/mL) [Median (IQR)]	2.6 (1.6 – 4.5)	2.6 (1.4 – 3.6)	3.1 (1.9 – 4.8)	0.06

* Dyslipidemia includes any of the following conditions: Total cholesterol≥ 200mg/dL, Triglycerides≥150 mg/dL, LDL≥130 mg/dL or HDL<40 mg/dL

- Prevalence of IR was 33% (95% Confidence Interval : 28 % - 38%)
- Those with IR were more likely to be overweight, have higher fasting blood sugar, dyslipidemic, hypertensive and on longer duration on HAART
- No association was found between GIP, IL6, IL10, TNF-α and Insulin Resistance
- Although leptin had a significant univariate association with IR (p<0.005), this was no longer true after adjusting for BMI





* CD4 category change : change from one category to the next, treated as a continuous variable

** BMI category change: change from one category to the next, treated as a continuous variable

Conclusion

- In a young cohort of PLWH on ART, more than 1/4th were insulin resistant
- IR was seen to be associated with other metabolic abnormalities
- GLP-1 was strongly associated with IR, mandating further investigation into the role of this incretin hormone in PLWH
- As C-peptide may not be as chemically inert as it was initially believed, our finding warrants the generation of hypotheses on its potential role not just a marker for IR but as its potential mediator, in future studies

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Contact details

Ivan Marbaniang

Byramjee Jeejeebhoy Government Medical College—Johns Hopkins University Clinical Research Site, Jai Prakash Narayan Road Pune– 411001, India

Email: ivanmarb@gmail.com