NICHD P1081: WEIGHT GAIN WITH RALTEGRAVIR VS EFAVIRENZ DURING PREGNANCY

Conrado Milani Coutinho [1], Meredith Warshaw [2], Geraldo Duarte [1], Alice Stek [3], Avy Violari [4], Cristina Barroso Hofer [5], Jaime Deville [6], James Samwel Ngocho [7], José Pilotto [8], Mario Dias Correa Jr [9], Trevon Fuller [6], Nahida Chakhtoura [10], Mark Mirochnick [11], Esaú João [12], for the NICHD P1081 study team.

[1]University of São Paulo at Ribeirão Preto, Ribeirão Preto, Brazil, [2]Harvard TH Chan School of Public Health, Boston, MA, United States, [3]University of Southern California, Los Angeles, CA, United States, [4]University of Witwatersrand, Johannesburg, South Africa, [5]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [6]University of California Los Angeles, Los Angeles, CA, United States, [7]Kilimanjaro Christian Medical Centre, Moshi, Tanzania, [8]Hospital Geral de Nova Iguaçu, Rio de Janeiro, Brazil, [9]Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, [10]National Institute of Child Health and Human Development, Bethesda, MD, United States, [11]Boston University, Boston, MA, United States, [12]Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil

BACKGROUND

- Gestational weight (wt) changes can affect pregnancy outcomes
- Integrase inhibitor use is associated with excessive wt gain and adverse metabolic effects in non-pregnant adults
- Wt gain with use of raltegravir (RAL) during pregnancy has not been described
- NICHD P1081: Phase IV randomized trial comparing virologic response with use of RAL vs efavirenz (EFV) in antiretroviral naïve pregnant women living with HIV
- Post-hoc exploratory analyses objectives: (1) to compare antepartum changes in wt and body mass index (BMI) between arms; (2) to examine associations between wt gain and adverse pregnancy outcomes (APO)

METHODS

- Population: 281 women with singleton pregnancies, 20-31 gestational weeks, on study for ≥4 weeks
- Wt/BMI analyzed as rate of change per week from entry to last measure prior to delivery (median rates on EFV vs RAL compared using Kruskal-Wallis tests)
- Low rate of wt gain defined as <0.18 kg/wk, normal rate between 0.18-0.58 kg/wk and high rate defined as ≥0.59 kg/wk (frequencies on EFV vs RAL compared using Fisher's exact test)

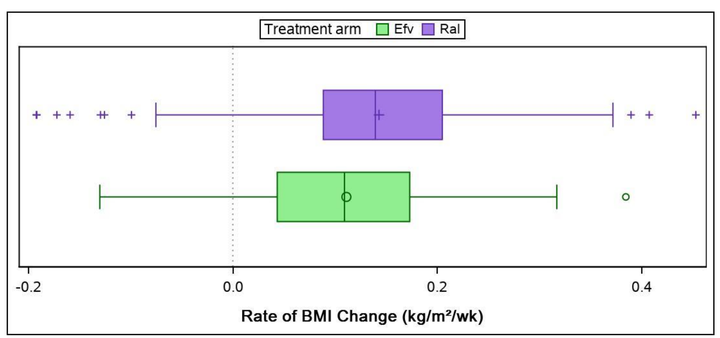

Figure 1. Antepartum rate of BMI change by treatment arm.

ARV-naïve pregnant women:

- On RAL were less likely than those on EFV to have low rates of weight gain and more likely to have high rates of weight gain
- With low versus normal rate of weight gain were significantly more likely to have SGA infants and meet the composite adverse pregnancy outcome

- Association between wt gain category and APO (stillbirth, neonatal death, preterm delivery <37 and <34 weeks, small and large for GA [SGA and LGA], or a composite APO) (Exact logistic regression analyses)
- Analyses used 2-sided 5% significance level

Table. Association of rate of antenatal weight gain with birth outcomes.

	N (column %) with outcome			Odds Ratio (95% Confidence Interval)			
Birth Outcome	Low rate (N=76)	Normal rate (N=158)	High rate (N=47)	Low vs. normal rate of weight gain	p-value	High vs. normal rate of weight gain	p-value
Composite outcome**	32 (44%)	35 (22%)	13 (28%)	2.7 (1.4, 5.2)	0.002	1.3 (0.6, 3.0)	0.55
Stillbirth	3 (4%)	0 (0%)	0 (0%)	8.2 (1.2, >999.9)	0.07	N/A	N/A*
Neonatal death	1 (1%)	1 (1%)	0 (0%)	2.1 (0.0, 165.3)	>0.99	N/A	N/A*
Preterm <37 weeks	7 (10%)	15 (9%)	7 (15%)	1.1 (0.4, 3.0)	>0.99	1.7 (0.5, 4.7)	0.43
Preterm <34 weeks	2 (3%)	3 (2%)	4 (9%)	1.5 (0.1, 13.8)	0.96	4.8 (0.8, 33.7)	0.10
Small for gestational age	21 (30%)	20 (13%)	7 (15%)	3.0 (1.4, 6.4)	0.003	1.2 (0.4, 3.2)	0.85
Large for gestational age	4 (6%)	16 (10%)	2 (4%)	0.5 (0.1, 1.8)	0.43	0.4 (0.0, 1.8)	0.34

* N/A: Not available (odds ratios and confidence intervals could not be estimated well due to very small numbers of events)
** Composite includes the occurrence of any of: stillbirth, neonatal death, preterm (<37 weeks) or small for gestational age (<10th percentile)

RESULTS

- Baseline characteristics were similar between EFV (N=137) and RAL (N=144) groups
- RAL-based ARV regimen was associated with significantly higher antepartum rate of wt gain (median 0.36 kg/wk vs. 0.29 kg/wk, p=0.01) and BMI increase (median 0.14 kg/m^2/wk vs. 0.11 kg/m^2/wk, p=0.01) compared to EFV-based treatment
- Women on RAL were less likely to have low rate of wt gain (18% vs. 36%) and more likely to have high rate of wt gain (21% vs. 12%) (p=0.001)
- Women with low rate of wt gain were significantly more likely to have SGA infants or to have composite APO than women with normal rate of wt gain (Table)
- There were no significant differences in rates of APO between women with high versus normal rate of wt gain

CONCLUSIONS

- Low rate of wt gain in this study was associated with adverse pregnancy outcomes and was less likely with RAL based treatment

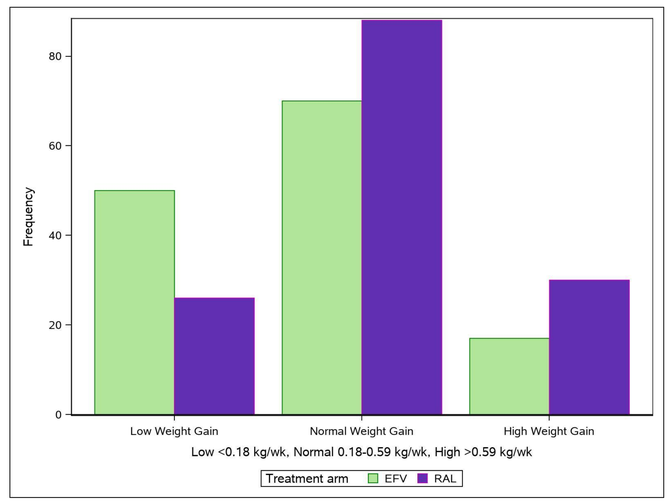

Figure 2. Antepartum rate of weight change by treatment arm.

ACKNOWLEDGEMENTS

- Research Collaborator: David E. Shapiro, Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA.
- Overall funding and support from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) through contract HHSN275201800001I, with co-funding and regulatory support from the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT), the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632 (IMPAACT LOC), UM1AI068616 (IMPAACT SDMC) and UM1AI106716 (IMPAACT LC). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.