

Effects of Western diet and pregnancy on liver triglycerides and oxidative stress

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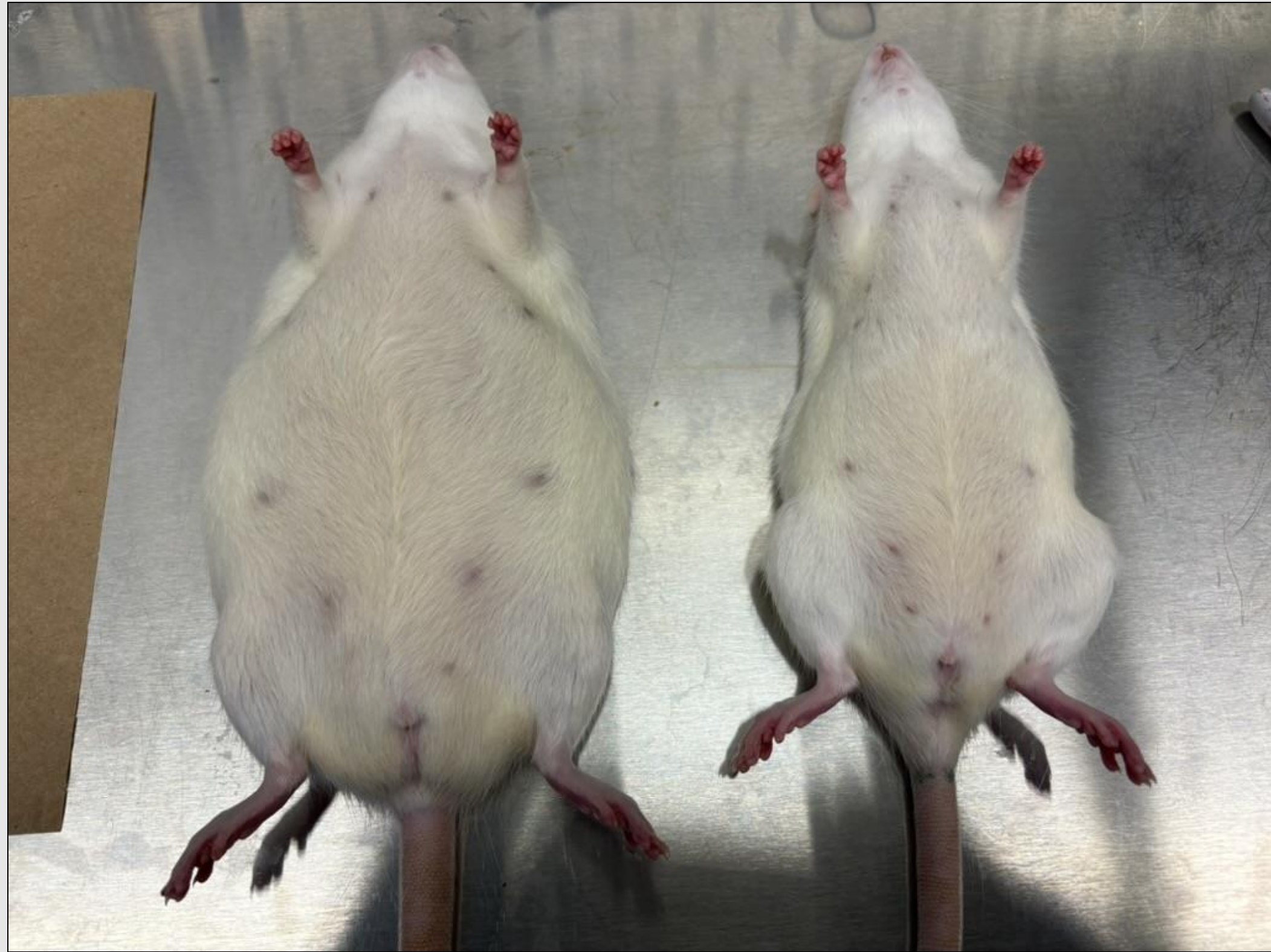


BACKGROUND

Maternal obesity is a growing problem worldwide and is associated with metabolic dysfunction-associated fatty liver disease (MASLD), systemic inflammation and oxidative stress. We previously showed that a high-fat, high-sucrose "Western" diet (WD) increases visceral adiposity in pregnant/non-pregnant female Wistar rats, and that pregnancy per se increases total fat stores, independent of diet (Coggin-Carr et al. BJOG 2022;129(S1):138-139). Interestingly, liver weight was increased by pregnancy but not WD; however, there was a diet*pregnancy interaction (p=0.034), wherein liver weight increased to a lesser degree in WD-fed dams (12.1±0.27g vs. 8.6±0.61g for non-pregnant WD) than control diet (CD)-fed dams (13.7±0.28g vs. 8.4±0.37g for non-pregnant CD). No such interactions were seen for other organ or fat depot weights. **Objective:** to determine effects of WD/pregnancy on hepatic triglyceride (TG) content and malondialdehyde (MDA) activity (lipid peroxidation product / marker of oxidative stress) and fasting glucose. **Design:** Animal study (2x2 design) with four groups: WD-fed pregnant (WD+P, n=10); WD-fed non-pregnant (WD-NP, n=10); CD-fed pregnant (CD-P, n=10); and CD-fed non-pregnant (CD-NP, n=10).

METHODS

Forty female Wistar rats (aged 78±1d, initial bodyweight 212±3g) received either WD (TestDiet 58V8, 20% sucrose, 45% fat) or CD (standard chow) for 71±2d prior to mating (n=20 each). Rats were co-housed with males overnight during estrus/pro-estrus. Diets were continued until necropsy on embryonic day (E)20 for dams (n=10 per diet) or equivalent age for non-pregnant rats (n=10 per diet). Before euthanasia, food was withheld for 12h and fasting blood glucose measured by glucometer (Freestyle Lite). Major organs and internal fat depots were weighed. Liver samples were homogenized for determination of TG content and MDA activity in duplicate using commercial assays (Cayman Chemical) by investigators blind to group allocation. Data were analyzed by two-way ANOVA with diet (WD/CD) and pregnancy (+/-) as fixed factors.



DIO Rodent Purified Diet w/45% Energy From Fat - Red		58V8
DESCRIPTION	NUTRITIONAL PROFILE ¹	
Diet Induced Obesity (DIO) Rodent Diet with 45% Energy From Fat. Dyed Red is a Purified Diet based on AIN-76A Semi-Purified Diet, Rat or Mouse 5800-B. See Van Heek et al., J. Clin. Invest. 99:385-390, 1997, for initial use of this formula. Originally manufactured as "D12451".	Protein, %	20.8
Intended for rodents in a laboratory setting.	Arginine, %	0.81
CAUTION: Contains a new animal drug for investigational use only in laboratory research animals or for tests in vitro. Not for use in humans.	Histidine, %	0.60
Storage conditions are particularly critical to TestDiet products, due to the absence of antioxidants to prevent oxidative rancidity. To provide maximum protection against possible changes during storage, store in a dry, cool location. Storage under refrigeration (2° C) is recommended. Maximum shelf life is six months. (If long term studies are involved, storing the diet at 2° C in a cooler may prolong shelf life.) Be certain to keep in air tight containers.	Isoleucine, %	1.11
	Leucine, %	2.02
	Lysine, %	1.69
	Methionine, %	0.60
	Cysteine, %	0.44
	Phenylalanine, %	1.11
	Tyrosine, %	1.18
	Threonine, %	0.90
	Tryptophan, %	0.26
	Valine, %	1.33
	Alanine, %	0.64
	Aspartic Acid, %	1.50
	Glutamic Acid, %	4.76
	Glycine, %	0.45
	Proline, %	2.75
	Serine, %	1.29
	Taurine, %	0.00
Product Forms Available*	Fat, %	23.6
1/2" Pellet	Cholesterol, ppm	197
1/2" Pellet, 2 kg Vac Sealed	Linoleic Acid, %	3.48
1/2" Pellet, Irradiated	Linolenic Acid, %	0.32
Meal	Arachidonic Acid, %	0.04
	Omega-3 Fatty Acids, %	0.32
	Total Saturated Fatty A	9.05
	Total Monounsaturated Fatty Acids, %	9.32
	Polysaturated Fatty Acids, %	3.63
	Fiber (max), %	5.8
*Other Forms Available On Request		
INGREDIENTS (%)		
Casein - Vitamin Tested		23.3060
Lard		20.6840
Sucrose		20.0920
Maltodextrin		11.6630
Dextrin		8.4530
Powdered Cellulose		6.8270
Soybean Oil		2.9130
Potassium Citrate, Tribasic Monohydrate		1.9230
Calcium Phosphate		1.5150
DIO Mineral Mix		1.1650
AIN-76A Vitamin Mx		1.1650
Calcium Carbonate		0.6410
L-Cysteine		0.3800
Choline Bitartrate		0.2330
FD&C Red No. 40		0.0500

RESULTS

	Control diet Non-pregnant	Western diet Non-pregnant	Control diet Pregnant	Western diet Pregnant	P value <i>Diet</i>	P value <i>Pregnancy</i>	P value <i>Interaction</i>
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Key Organ Weights (g)

Pancreas	1.19 ± 0.071	1.16 ± 0.070	1.17 ± 0.032	1.16 ± 0.040	0.690	0.864	0.819
Liver	8.09 ± 0.295	8.56 ± 0.293	13.7 ± 0.353	12.1 ± 0.347	0.126	<0.001	0.005
Spleen	0.59 ± 0.027	0.67 ± 0.025	0.75 ± 0.023	0.79 ± 0.023	0.012	<0.001	0.440
Kidney	0.95 ± 0.016	1.01 ± 0.022	0.99 ± 0.018	0.96 ± 0.017	0.463	0.866	0.013
Adrenal	0.04 ± 0.002	0.04 ± 0.002	0.06 ± 0.002	0.05 ± 0.001	0.441	0.387	0.514
Ovary	0.07 ± 0.003	0.07 ± 0.003	0.10 ± 0.003	0.10 ± 0.003	0.722	<0.001	0.780

Fat Depot Weights (g)

Retroperitoneal	4.11 ± 0.341	10.8 ± 1.398	6.81 ± 0.427	12.7 ± 0.627	<0.001	0.003	0.591
Parametrial	6.12 ± 0.510	14.2 ± 1.848	8.59 ± 0.544	14.8 ± 0.794	<0.001	0.127	0.348
Mesenteric	2.16 ± 0.171	6.62 ± 1.346	4.02 ± 0.253	5.97 ± 0.314	<0.001	0.332	0.046
Inguinal	0.85 ± 0.056	2.31 ± 0.307	2.19 ± 0.098	2.90 ± 0.115	<0.001	<0.001	0.025

Laboratory Parameters

Hepatic malonaldehyde activity (µM)	17.7 ± 1.160	21.5 ± 2.315	18.9 ± 1.630	20.6 ± 2.677	0.191	0.936	0.632
Hepatic triglyceride content (mg/g)	39.2 ± 4.585	64.3 ± 4.341	70.7 ± 6.122	95.5 ± 13.13	0.003	<0.001	0.984
Fasting glucose (mg/dl)	58.2 ± 1.948	60.8 ± 1.535	42.6 ± 1.337	47.7 ± 2.054	0.036	<0.001	0.479
Fasting plasma insulin (ng/ml)	0.25 ± 0.054	0.59 ± 0.109	0.44 ± 0.047	0.82 ± 0.131	<0.001	0.033	0.858
Homeostatic model assessment of insulin resistance [HOMA-IR]	0.39 ± 0.072	1.54 ± 0.648	0.80 ± 0.094	1.29 ± 0.269	<0.001	0.623	0.602

CONCLUSION

Metabolic dysfunction in this rat model of maternal obesity is characterized by elevated fasting glucose and significantly increased hepatic TG content, despite relatively lower liver weight compared to healthy rat pregnancies