Circulating levels of Eotaxin-1, -2, and -3 chemokines in morbid obesity and 1 year follow up after bariatric surgery

H. Arefanian[1], F. Al-Asfar[2], E. Al-Ozairi[3], S. Al-Beloushi[1], E. Al-Shawaf[1], S. Kumari[1], S. Sabau[3], A. Al-Hubail[3], J. Tuomilehto[4].

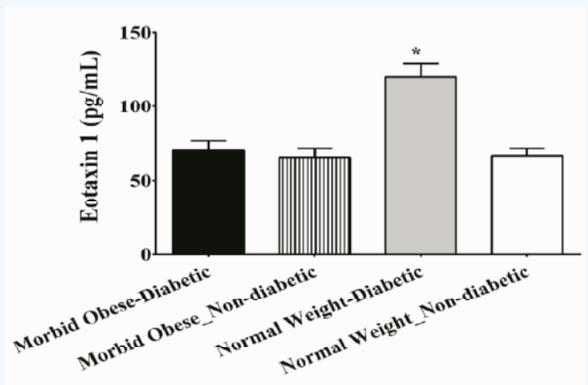
[1]Dasman Diabetes Institute, Islet Biology Unit- Research Division. [2]Kuwait University, Department of Surgery- Faculty of Medicine. [3]Dasman Diabetes Institute, Medical Division.[4]Dasman Diabetes Institute, Research Division.
Kuwait City, Kuwait.

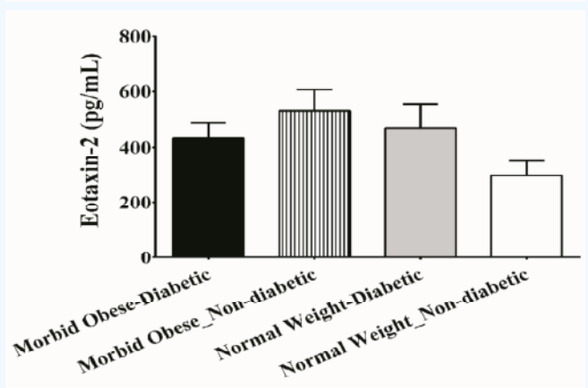
Background: Chemokines as one of the important mediators in immune cell infiltration have been hypothesized to be involved in macrophage infiltration into adipose tissue in obesity and might therefore play an important role in the development of obesity-related disorders like type 2 diabetes. Eotaxins (eosinophil chemotactic proteins) namely Eotaxin1 (CCL11), Eotaxin2 (CCL24), and Eotaxin3 (CCL26) belong to CC chemokine family, in addition to their important role in asthma, recent reports showed their association to obesity. However, the role of these chemokines is poorly understood.

Aim: Our aim was to study any possible kinetic change and association between circulatory level of Eotaxins (Eotaxin1, Eotaxin2, and Eotaxin3), obesity and type 2 diabetes before and after Laparoscopic Sleeve Gastrectomy (LSG).

Method: 38 morbidly obese participants (16 diabetic and 22 non-diabetic) with a BMI ≥ 40 kg/m^2 underwent LSG, while 32 normal weight subjects (18 diabetic and 14 non-diabetic) with a BMI < 25 kg/m^2 were recruited as controls. We compared the basal levels of circulatory Eotaxins (pg/mL) in morbid obese participants before LSG to the basal levels in normal weight subjects. The correlation between levels of these chemokines and other clinical and biochemical parameters was also studied. Some of the morbidly obese participants were further examined at the time points of 7, 15, 30, 60, 90,180 and 360 days postoperatively.

Fig 1: At baseline, levels of Eotaxin1 was significantly (*$p < 0.0001$) higher in normal weight diabetic subjects (n=18, 120.1±8.78) compared to other groups, including morbid obese-diabetics (n=16, 70.63±6.17), morbid obese non-diabetics (n=22, 65.47±6.23) and normal weight non-diabetics (n=14, 66.52±5.17). Eotaxin2 levels showed no significant difference between all study groups. However, Eotaxin3 was significantly higher (**$p < 0.0003$) in morbid obese participants (diabetics; 48.42±4.80, and non-diabetics; 48.93±4.06) compared to normal weight participants (diabetics; 27.47±3.94 and non-diabetics; 20.42±1.93).





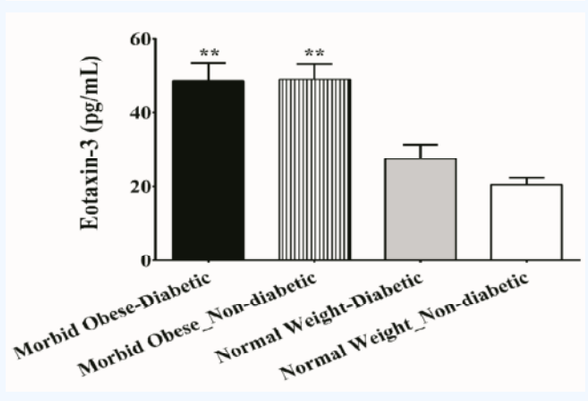
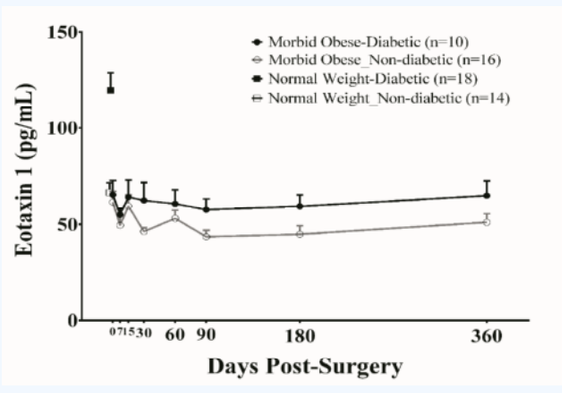
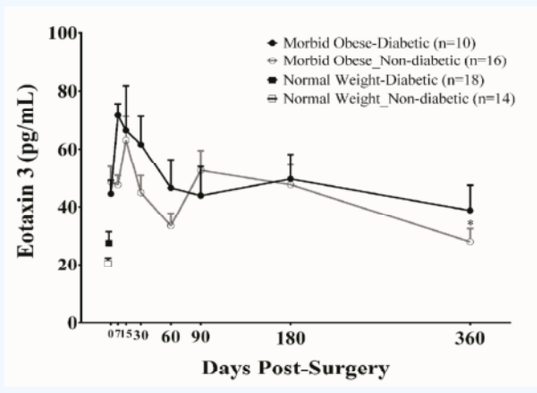
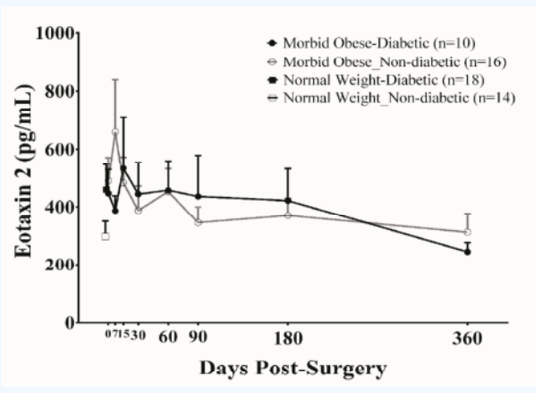


Fig 2: After one year of LSG, the level of Eotaxin3 was significantly ($p < 0.02$) reduced in morbid obese non-diabetic (29.42±5.71), reaching a level that is comparable to normal weight participants. A similar pattern of reduction, but no significance was observed in the level of Eoatxin3 (37.94±10.87) in morbid obese diabetic participants after one year of LSG.







			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
Morbid Obese Subjects	Eotaxin1	r	.219	.135	.158	.233	-.314	.303	.095	.061	-.126	.014	.005	-.164
		p	.187	.419	.344	.160	.055	.065	.572	.715	.450	.934	.977	.324
	Eotaxin2	r	.060	.023	.145	-.063	-.331*	.020	-.257	-.169	-.224	-.296	-.166	.081
		p	.721	.893	.384	.705	.042	.906	.119	.309	.176	.072	.319	.629
	Eotaxin3	r	.255	.146	.244	.086	-.172	.208	-.173	-.143	.005	-.193	.092	-.160
		p	.122	.382	.140	.607	.302	.210	.299	.391	.978	.245	.582	.338
			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
Normal Weight Subjects	Eotaxin1	r	-0.02	0.01	0.31	0.19	0.10	.56**	.591**	.249	-.013	.63**	-0.03	-0.27
		p	0.93	0.94	0.09	0.27	0.59	<0.0008	<0.0004	.170	.943	<0.0001	0.88	0.14
	Eotaxin2	r	.367*	0.22	-0.03	0.16	-0.02	0.23	0.23	.084	.051	0.05	0.14	0.02
		p	0.04	0.23	0.87	0.39	0.93	0.21	0.20	.648	.780	0.79	0.45	0.92
	Eotaxin3	r	0.11	0.10	-0.07	0.07	0.08	0.19	0.13	.108	.062	0.14	0.19	-0.06
		p	0.56	0.58	0.69	0.69	0.65	0.29	0.47	.556	.736	0.45	0.30	0.76
			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
Diabetic Subjects	Eotaxin1	r	-.629**	-.56**	-.50**	0.09	-.50**	-0.01	-0.07	-.539**	-.621**	0.12	-.43**	0.05
		p	<0.0001	<0.0006	<0.002	0.61	<0.002	0.96	0.70	.001	.000	0.50	<0.01	0.77
	Eotaxin2	r	0.03	-0.01	-0.02	-0.04	-0.23	0.03	-0.06	.054	.039	-0.25	-0.04	0.08
		p	0.88	0.98	0.92	0.82	0.19	0.88	0.73	.763	.825	0.16	0.82	0.65
	Eotaxin3	r	.56**	.61**	.60**	-0.08	.57**	.469**	0.12	.517**	.568**	-0.02	.57**	-0.07
		p	<0.0005	<0.0001	<0.0001	0.64	<0.0004	<0.004	0.51	.002	.000	0.93	<0.0004	0.71
			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
Non-diabetic Subjects	Eotaxin1	r	.056	-.089	-.043	.071	-.304	.216	.002	-.053	-.065	-.204	-.088	.111
		p	.745	.605	.806	.682	.072	.205	.990	.758	.707	.232	.612	.520
	Eotaxin2	r	.376*	.387*	.337*	.190	.120	.288	-.147	.076	.202	-.205	.201	-.022
		p	.024	.020	.044	.266	.485	.088	.394	.659	.238	.230	.241	.898
	Eotaxin3	r	.685**	.590**	.638**	.276	.34*	.513**	.022	.459**	.498**	.073	.583**	-.369*
		p	.000	.000	.000	.103	<0.039	.001	.898	.005	.002	.674	<0.0002	<0.02

Table 1: Spearman correlation analysis of baseline levels of Eotaxin chemokines.

Conclusion: We observed an association between the circulatory levels of Eotaxin chemokines (inverse association of Eotaxin-1 and direct association of Eotaxin-3), with the level of obesity and markers of low grade chronic inflammation before and after LSG.

Acknowledgment: This study was funded by Kuwait Foundation for the Advancement of Sciences (KFAS). CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT03038373.

References:

1. Dalmas,E, Rouault,C, Abdennour,M, Rovere,C, Rizkalla,S, Bar-Hen,A, Nahon,JL, Bouillot,JL, Guerre-Millo,M, Clement,K, Poitou,C: Variations in circulating inflammatory factors are related to changes in calorie and carbohydrate intakes early in the course of surgery-induced weight reduction. *Am.J.Clin.Nutr.* 94:450-458, 2011
2. Gentili,A, Zaibi,MS, Alomar,SY, De Vuono,S, Ricci,MA, Alaeddin,A, Siepi,D, Boni,M, Vaudo,G, Trayhurn,P, Lupattelli,G: Circulating Levels of the Adipokines Monocyte Chemotactic Protein-4 (MCP-4), Macrophage Inflammatory Protein-1beta (MIP-1beta), and Eotaxin-3 in Severe Obesity and Following Bariatric Surgery. *Horm.Metab Res.* 48:847-853, 2016