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Role of Expression of Leptin Receptors in Ovarian Cancer in Babylon Province

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Abstract

Background: one of the incessant gynecological tumors is ovarian cancer, with most of patients being analyzed at a late stage. The five-year survive around 30%. Generally, it present at late stage, with a low survival probability, due to a lack of good screening tools. The objective: study the association of deregulated leptin receptor-mediated signaling with ovarian tumor.

Methods: In this case, control study, which involved 140 participants, 100 patients with ovarian tumor and 40 control. The Automated Slide Stainer (Ventana Discovery XT) was used to stain IHC.Specimens stained for LEPR were digitized at 20.

Results: There was significant difference among them regarding expression of leptin receptor ($p<0.05$). There was significant difference between malignant form and controls ($p<0.05$) but insignificant difference between benign and borderline type and control group ($p>0.05$).72.5% with Ovarian cancer had positive leptin receptor while only 40% in control group. Multinomial regression was done, negative leptin IHC had significant lower odds ratio in Serous Epithelial Ovarian Cancer when compared with healthy control. Negative leptin signal had protective effect for Serous Epithelial Ovarian Cancer (odds ratio =0.246, [0.095-0.638]). Borderline tumor and Benign Ovarian Tumor had also lower odds ratio for negative leptin IHC ($p>0.05$). Absence of leptin receptor had protective role from ovarian cancer.

Conclusion: Elevated levels of leptin receptors have been associated to an increased risk of ovarian cancer.These findings could aid in the development of ovarian cancer screening and treatment options.

Keywords: Expression, Leptin Receptors, ovarian Cancer, Babylon province

1. INTRODUCTION

Gynecological diseases incorporate ordinarily happening malignancies like carcinomas of cervix, endometrium cancer and ovarian cancer. These diseases were responsible for above 16% of all malignancy[1]. Ovarian malignancy is quite possibly the most well-known gynecological cancer worldwideand most of patients are late in diagnoses. The endurance paces of ovarian disease are roughly 30% [2,3]. Without successful screening strategies, women who are determined to have ovarian malignancy regularly present at a high-level stage related with a helpless endurance rate [2]. Along these lines, preventive ways are needed to decrease mortality rate and offer early diagnosis[4].One of the most `important risk factor was obesity[5]. As of late, epidemiological investigations have shown that stoutness is related with an expanded danger of ovarian malignant growth [6]. A few examiners detailed that obesity related with reduced prediction [7,8], the specialists reasoned that higher bodyweight was related with expanded danger of fringe serous, second rate intrusive serous, obtrusive endometrioid, and intrusive mucinous cancers [9] and increase risk of serous type[10]. Leptin is protein. Fat tissue responsible for it synthesis [11]. It supports the state of insulin resistance. Leptin acts through receptors on cell membrane [12]. Leptin receptor (Ob-R) has a place with class I cytokine receptor bunch encoded by Ob and is communicated in a wide range of tissues. Leptin controls different flagging pathways in numerous human malignant growths. "JAK2/STAT3 (Janus kinases/transducer and activator of transcription3), IRS1/2-PI3K/AKT (Insulin receptor substrate/phosphatidylinositol 3-Kinase/Protein kinase B), SHP2/ERK (Src Homology Phosphatase 2/Extracellular Signal-Related Kinase), COX-2 (CyclooxygenaThe JAK-STAT, PI3-Kinase-AKT, and MAP kinase signaling pathways are all tinkered with by leptin-receptor interaction" [13, 14].As of late, liberated leptin-interceded flagging has been displayed in numerous diseases including ovarian malignancy. Various examinations have shown a connection among stoutness and carcinogenesis of various

malignant growths by means of leptin liberated flagging pathways [15]. The target of this review was to decide if the job of liberated leptin receptor-interceded flagging related with ovarian growth.

2. METHODS

In this case, control study, which involved 140 participants, 100 patients with ovarian tumor and 40 control.The recently determined ovarian growth to have histologically affirmed various sorts of growth (Benign Ovarian Tumor, Serous Epithelial Ovarian Cancer and Borderline cancer. Cancer grade was characterized as grades 1 through 3: grade 1 meant all around separated growths, grade 2 signified modestly separated cancers, and grade 3 meant ineffectively separated growths. Assortment of documented ovarian growth examples and tissue microarray development: Tumor blocks as well as slides were gathered from clinics after composed assent was gotten from concentrate on members.

3. IMMUNOHISTOCHEMISTRY

The Ventana Discovery XT Automated Slide Stainer was used for all IHC staining (Ventana Medical Systems, Inc., Tucson, AZ, USA).

On an Olympus VS120 whole slide scanner, examples stained for LEPR were digitized at 20. (Olympus Corporations, Central Valley, PA, USA). Figure 1 shows examples of the resultant IHC staining for each biomarker on WCHS TMA specimens. To fabricate a bespoke work procedure and perform quantitative evaluation of IHC articulation on each tissue center, a computerized pathology examination stage (VisioPharm, Hoersholm Denmark) was used. Inside the viable staining region, quantitative IHC articulation data were considered for as powerful staining force (ESI) (ESA). Curiosities like tissue collapse were physically prohibited from being measured. A board-certified pathologist (MC) also used TMA-AID to grade IHC articulation for LEPR of each tissue center stained.

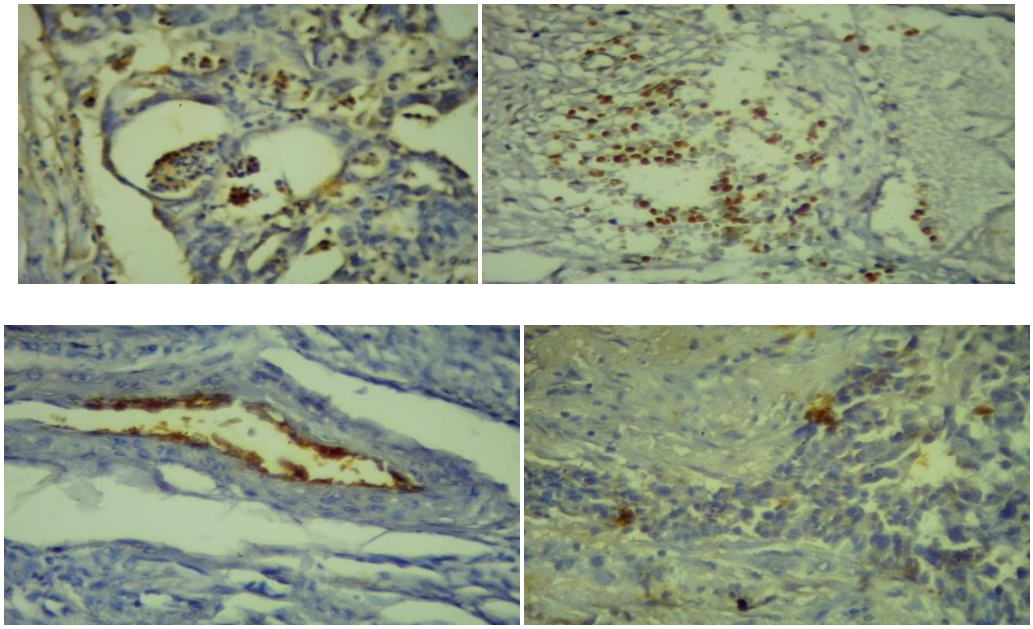

Figure1: The overexpression of leptin protein in surface epithelial ovarian cancers can be seen under a microscope. Mayer's hematoxylin was used to counterstain the DAB chromogen (brown) stain.

4. STATISTICAL ANALYSIS

SPSS version 23 was used,s *t* tests and Chi test was used. In addition,Multinomial regression was done for associations between leptin receptor with overain tumor.$P < 0.05$ was considered statistically significant.

5. RESULTS

Table 1 shows the Mean ±SD of age in patientswith ovariantumor. There no significant difference in age between studied group(p>0.05).

Table 1: Mean ±SD of age in patients with ovarian tumor.

Studied groups	N	(Age/ Year) Mean± Std. Deviation	Range		P-value
			Mini.	Maxi.	
A.H. Control	40	37.33±7.556	27	54	0.241
'Benign Ovarian Tumor'	40	36.30±7.83	19	55	
'Serous Epithelial Ovarian Cancer'	40	39.00±8.77	25	57	
'Border line tumor'	20	41.90 ±10.13	29	57	

In terms of Malignant Serous Epithelial Ovarian Tumor Histological Grade, nearly half of them had poor differentiation (42.5%), 30 had moderate differentiation, and the rest had well differentiation**.**

Table 2: The tumor grading system for "serous epithelial ovarian" tumors.

'Ovarian Cancer Grades(Differentiated)'	N(%)
Well (I)	11(27.5)
Moderately (II)	12(30)
Poorly (III)	17(42.5)
Total	40(100.0)

Table 3 shows theDistribution of Leptin Signals with Ovarian Tumors. There was significant difference among them regarding expression of leptin receptor (p<0.05) .There was significant difference between malignant type and control group (p<0.05) but insignificant difference between benign and borderline type

and control group (p>0.05).72.5% with Ovarian cancer had positive leptin receptor while only 40% in control group.

Table 3: Distribution of *Leptin* Signals with Ovarian Tumors.

Leptin-IHC		Studied groups				Chi-Square (P-value)
		A.H. Control	Benign tumor	Border line tumor	Ovarian cancer	
Positive	N	17	22	6	29	0.042*
	%	40%	55%	30%	72.5%	
Negative	N	23	18	14	16	
	%	60%	45%	70%	27.5%	
Total	N	40	40	20	40	
	%	100%	100%	100%	100%	
(P-value)			0.244 NS	0.321 NS	0.042 S	

P<0.05 was significant

Multinomial regression was done, negative leptin IHC had significant lower odds ratio in Serous Epithelial Ovarian Cancer when compared with healthy control. Negative leptin signal had protective effect for Serous Epithelial Ovarian Cancer (odds ratio =0.246, [0.095-0.638]). Border line tumor and Benign Ovarian Tumor had also lower odds ratio for negative leptin IHC (p>0.05). Absence of leptin receptor had protective role from ovarian cancer.

Table 4: Multinomial regression analysis for leptin IHC in different ovarian tumor against control group

Group		P value	Odds ratio	"95% Confidence Interval for Odds ratio"	
				Lower Bound	Upper Bound
Serous Epithelial Ovarian Cancer	Leptin-IHC Negative	0.004	0.246	0.095	0.638
	Leptin-IHC Positive	.	.	.	.
Border line tumor	Leptin-IHC Negative	0.670	0.739	0.184	2.965
	Leptin-IHC Positive	.	.	.	.
Benign Ovarian Tumor	Leptin-IHC Negative	0.265	0.605	0.250	1.463
	Leptin-IHC Positive	.	.	.	.

a. The reference category is: Control

b. This parameter is set to zero because it is redundant

6. DISCUSSION

Many studies suggest that leptin is overexpressed in various disease cells and plays a role in the progression and progression of a variety of cancers, including colon, gastric, endometrial, and breast tumors [16–20]. These findings were also supported by preliminary evidence that leptin can stimulate development and prevent apoptosis in a variety of cell malignancy models [21–23]. Stoutness is a risk factor for ovarian malignant development in postmenopausal women, according to an ongoing epidemiological study [24].

Accordingly, we inspected the of leptin receptor in 140 examples. Our information shows that there was huge contrast among them in regards to articulation of leptin receptor (p<0.05) .There was critical distinction between harmful sort and control bunch (p<0.05) however immaterial contrast among harmless and marginal sort and

control bunch (p>0.05).72.5% with Ovarian malignancy had positive leptin receptor while just 40% in control bunch.

The effect of leptin on the delivery of histone deacetylases (HDAC) in the ovaries remains unknown. It changes food intake and body weight [25].

Tchio et al. [26]showed that leptin could just directly circle back to HDAC4 and HDAC5. Notwithstanding, leptin can in a roundabout way influence other HDACs by affecting microRNAs; leptin can make miR21 (oncogenic microRNA21), which can expand HDAC3 enunciation, and the consolidated movement of these parts causes sickness cell augmentation. HDAC1 pharmacological hindrance, which is connected to chemoresistance in ovarian illness cells, can stretch out development cell affectability to cells that aren't powerless[27]Nebbioso et al. [28] were able to reduce the declaration of leptin receptor characteristics in adipocytes. Selectiveleptin receptor antagonists 'SHLA and Lan-2', may have assistances in the of ovarian disorders treatmentbecause they can diminishHDAC levels.

Chen et al display that proteins cyclin D1 and Mcl-1 was animates the cooperation by leptin. It advances cell development and restrains apoptosis in ovarian malignant growth cells[29].

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