

# •Correlation of midkine levels in serum and thyroid nodules with histopathological, haematological and radiological variables



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## Background

Midkine (MK), a novel heparin-binding growth factor. It plays critical roles in a variety of biological phenomena such as carcinogenesis, inflammation, cellular proliferation, survival, migration of cellular functions, angiogenesis and fibrinolysis. We aimed to evaluate the value of serum (SMK) and nodular (NMK) midkine levels in thyroid nodules to predict malignancy and to investigate the probably association of MK levels with ultrasonographic features.

## Materials/Methods

A total of 80 patients (56 women, 24 men) with thyroid nodules were included in this prospective study. Complete blood count, thyroid function tests, fine needle aspiration biopsies and ultrasonographic evaluation were made routinely. In addition, levels of SMK and NMK were measured. Any possible correlations between SMK, NMK and biochemical or radiological variables under investigation were sought.

## Results

The mean age of the study group was 51.9±14.4. Demographic and clinical characteristics in relation to serum (SMK) and nodular midkine (NMK) concentrations were shown in Table 1.

Both SMK and NMK were found to be higher in hypoechoic nodules with an irregular border and without an halo. Serum MK levels were significantly higher in nodules containing microcalcifications than the macrocalcification or without calcification (p=0.001). Serum MK levels were higher in patients with differentiated thyroid carcinoma (1.04 ng/ml) than patients with follicular adenoma or nodular hyperplasia (0.63 ng/ml) (p=0.066) (Table 2) SMK levels seemed to correlate with NMK levels (SMK 0.63 ng/ml vs 1.04 ng/ml and NMK 0.55 ng/ml vs 0.55 ng/ml, r =0.54, p <0.001).

**Table 1** Demographic and clinical characteristics in relation to serum (SMK) and nodular Midkine (NMK) concentrations

Feature		SMK	NMK
Gender	F/M	0.60 (0.63 (0.30-4.97)	0.52 (0.68 (0.35-1.73)
	p Value	0.912	0.223
Age(years)	<40	0.67 (0.37-4.97)	0.56 (0.38-1.73)
	40-59	0.60 (0.30-2.77)	0.52 (0.35-1.45)
	≥60	0.60 (0.40-2.03)	0.55 (0.37-0.82)
	p Value	0.396	0.298
BMI (kg/m <sup>2</sup> )	<30	0.60 (0.30-1.57)	0.53 (0.35-0.82)
	≥30	0.63 (0.40-4.97)	0.55 (0.40-1.73)
	p Value	0.280	0.107
TSH (µIU/ml)	<0.4	0.57 (0.33-2.03)	0.52 (0.35-0.82)
	0.4-4	0.63 (0.30-4.97)	0.53 (0.35-1.73)
	>4	0.63 (0.50-1.37)	0.58 (0.43-0.62)
	p Value	0.467	0.529

**Table 2** Relationship between SMK/NMK concentrations and fine needle aspiration cytology / histopathology results.

		Serum Midkine	Nodular Midkine
Cytopathology	Benign (n=71)	0.60 (0.30-4.97)	0.52 (0.35-1.73)
	Suspicious/ Malignant (n=9)	1.37 (0.50-4.13)	0.62 (0.43-1.50)
	p Value	0.005	0.015
Histopathology	Follicular adenoma /Nodular hyperplasia (n=28)	0.63 (0.30-4.13)	0.55 (0.35-1.50)
	Differentiated Thyroid Cancer (n=6)	1.04(0.48-1.53)	0.57 (0.48-0.80)
	p Value	0.066	0.341

## Conclusion

Results of the current study showed that both SMK and NMK were indicators of highly malignant/suspicious thyroid cytopathology and also correlate well with sonographic features of thyroid malignancy. We suggest that MK may serve as a novel biomarker, in conjunction with the cytopathological results in preoperative assessment of thyroid nodules.