Peripheral Sensory Neuropathy and Impaired Angiogenesis in Diabetes Patients in Ghana

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Introduction

- **Background**: Impaired angiogenesis may be amongst the possible mechanism underlining the development of peripheral sensory neuropathy (PSN) in type 2 diabetes (T2DM) patients.[1] Angiogenesis is regulated by circulating vascular growth factor, notably, angiopoietin (Ang)-1, Ang-2 and vascular endothelial growth factor (VEGF).[2]
- **Aim**: We studied the relationship between PSN and circulating vascular growth factors, Ang-1, Ang-2 and VEGF in T2DM patients.

Method

- In a case-control design, Horwell's Neurothesiometer was used to assesse vibration perception threshold (VPT) in 107 T2DM patients and 93 non-diabetes controls.
- PNS was defined as VPT≥25V.
- Fasting blood was collected to measure serum levels of Ang-1, Ang-2 and VEGF by ELISA.

Results

- Compared to non-diabetes subjects, T2DM patients have greater arterial stiffness and PSN despite similar age, gender distribution, BMI & brachial BPs (Table 1).
- In non-diabetes subjects, Ang-1 and Ang-2 levels were decreased in PSN patients while VEGF levels were increased. No difference in these factors were observed in T2DM patients (Fig. 1 – 3)
- VPT correlated positively with VEGF (r=0.22, p=0.003) and negatively with Ang-1 (r=-0.17, p=0.024).
- In logistic regression models, PSN was associated with decreased change in odds of Ang-1 and increased change in odds of VEGF in unadjusted and age- gender-adjusted models (Table 2).

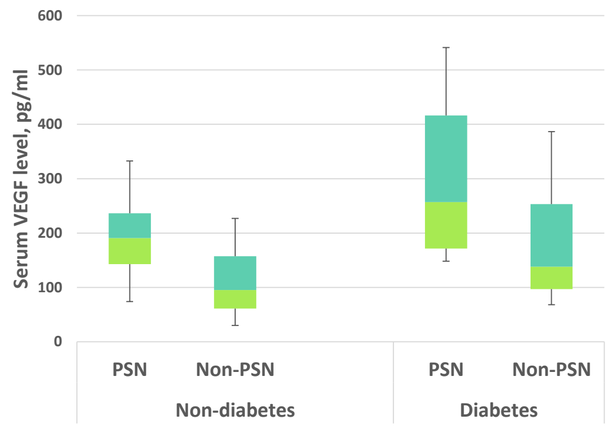

Fig. 3 Comparison of serum VEGF levels by PSN status

Table 1 clinical features of study subjects

	T2DM	Non-DM	p
Females	48 (44.9)	49 (56.3)	0.15
Age	53.7±10.1	54.6±10.3	0.54
BMI	28.9±5.9	29.4±5.5	0.57
WHR	0.92±0.07	0.9±0.14	0.38
SBP	141±26	135±34	0.17
DBP	83±13	82±14	0.59
Pulse BP	59±14	58±13	0.48
Heart rate	75±13	65±19	**<0.01**
PWVao	9.3±1.3	7.8±1.1	**0.03**
AIx	24.7±13.8	38.3±13	**<0.01**
CAVI	8.9±1.5	7.1±1.2	**0.01**
VPT	12.1±7.8	7.3±3.8	**<0.01**
PSN	22 (21.4)	9 (9.3)	**<0.01**

Table 2 Association between Vascular Growth Factors and PSN

	Logistic regression model		
	Growth Factor	Odds ratio (95% CI)	p
Crude model	**logAng-1**	**0.53 (0.16 – 0.92)**	**0.02**
	logAng-2	0.91 (0.49 – 1.69)	0.76
	logVEGF	**5.51 (1.53 – 9.81)**	**<0.01**
Model 1	**logAng-1**	**0.64 (0.31 – 0.96)**	**0.04**
	logAng-2	0.94 (0.49 – 1.77)	0.84
	logVEGF	**3.95 (1.08 – 7.44)**	**0.02**
Model 2	logAng-1	0.42 (0.18 – 0.83)	0.07
	logAng-2	0.93 (0.54 – 1.69)	0.81
	logVEGF	2.65 (0.82 – 4.85)	0.09

Model 1= Age and gender adjusted
Model 2= Model 1 plus diabetes & hypertension status, BMI, systolic BP, heart rate, cigarette smoking, alcohol intake, total and HDL cholesterol.

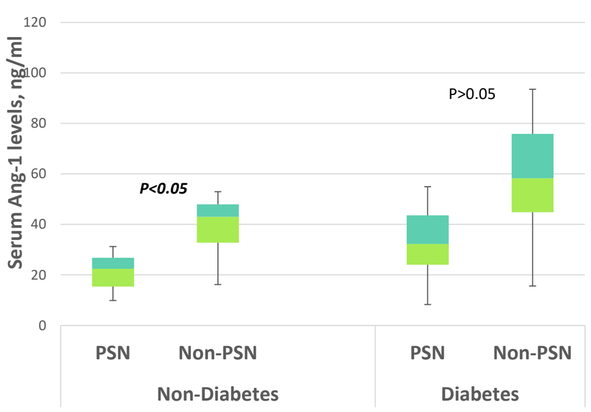

Fig. 1 Comparison of serum angiopoietin-1 levels by PSN status

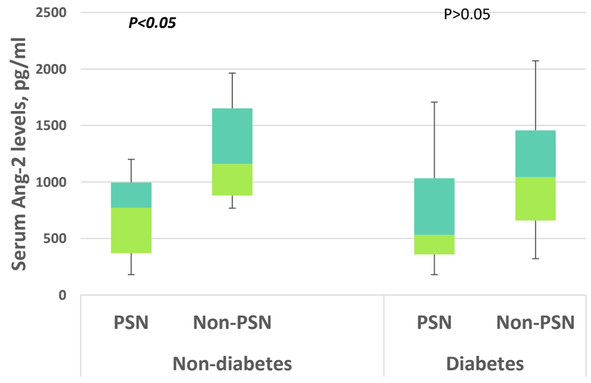

Fig. 2 Comparison of serum angiopoietin-2 levels by PSN status

References

1. Kim H, Kim JJ, Yoon Y-s. Emerging Therapy for Diabetic Neuropathy: Cell Therapy Targeting Vessels and Nerves. Endocrine, metabolic & immune disorders drug targets. 2012;12(2):168-78.
2. Fagiani E, Christofori G. Angiopoietins in angiogenesis. Cancer Lett. 2013;328(1):18-26. Epub 2012/08/28.

Conclusion

- PSN was associated with decreased in vascular growth factors, mostly in non-diabetes subjects.
- Ang-1 and VEGF decreased in PSN patients in age and gender adjusted models, but not in fully adjusted models, implying that there are other factors that mediates the association between PSN and vascular growth factors.