مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد السادس والعشرون - المجلد السادس - علوم الكيمياء - كانون أول 2025 م
doi.org/10.52866/esj.2025.06.26.22

Association between Serum Decorin and other Biochemical Parameters in Iraqi Type 2 diabetic patients with Nephropathy

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Abstract:

Decorin modulates the TGF-β pathway, implicated in diabetic nephropathy progression to end-stage kidney disease (ESKD). This study evaluated serum decorin levels and other biochemical parameters in diabetic nephropathy patients to assess potential links with disease development in type 2 diabetes mellitus (T2DM). 150 participants were divided into: healthy controls (G1, n=50), T2DM without nephropathy (G2, n=50), and T2DM with nephropathy (G3, n=50). HbA1c, fasting blood glucose (FBG), cholesterol, triglycerides, HDL, insulin, urea, creatinine, and decorin were measured. the Compared to G1, G2 and G3 had significantly higher FBG, HbA1C, cholesterol, triglycerides, urea, and creatinine, and significantly lower HDL. G2 also had significantly lower insulin than G1. Between G2 and G3: total cholesterol, triglycerides, and urea were significantly higher in G3; FBG, HbA1C, creatinine, HDL, and insulin showed no significant difference. Critically, serum decorin level was significantly elevated in G2 compared to G1 and showed a substantial increasing in G3 compared to G2. finally Elevated decorin levels are associated with T2DM and further increase with nephropathy, suggesting decorin's significant role in diabetic nephropathy development. Decorin may serve as a valuable biomarker for predicting the progression of diabetic kidney disease.

Keywords: Diabetic Nephropathy, Decorin , chronic kidney disease, Biochemical Markers & Insulin .

العلاقة بين بروتين ديكورين المَضلِيّ وبين المُعَامِلات الكيميائية الحيوية الأخرى لدى مرضى السكري من النوع الثاني العراقيين المصابين باعتلال الكلى

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مستخلص:

يُعدِّل بروتين الديكورين (Decorin) مسار عامل النمو المحول بيتا (TGF-β)، الذي يُعزَى إليه دور في تقدم اعتلال الكلية السكري إلى مرحلة المرض الكلوي في المرحلة النهائية (ESKD) . هدفت هذه الدراسة إلى تقييم مستويات بروتين الديكورين في مصل الدم ومستويات المعايير الكيموحيوية الأخرى لدى مرضى اعتلال الكلية السكري، لتقييم الروابط المحتملة مع تطور المرض عند مرضى السكري من النوع الثاني (T2DM). قُسِّم 150 مشاركًا إلى: مجموعة ضابطة سليمة (G1، عدد=50)، ومرضى مصابين بالسكري من النوع الثاني دون اعتلال كلوي (G2، عدد=50)، ومرضى مصابين بالسكري من النوع الثاني مع اعتلال كلوي (G3، عدد=50). تم قياس: الهيموغلوبين السكري (HbA1c) ، وسكر الدم الصائم (FBG)، والكوليسترول الكلي، والدهون الثلاثية، والكوليسترول عالي الكثافة (HDL) ، والأنسولين، واليوريا، والكرياتينين، وبروتين الديكورين.مقارنةً بالمجموعة الضابطة (G1)، سجَّلت مجموعتي مرضى السكري (G2) و (G3) مستويات أعلى ذات دلالة إحصائية (P≤0.05) في: سكر الدم الصائم (FBG)، والهيموغلوبين السكري (HbA1C) ، والكوليسترول الكلي، والدهون الثلاثية، واليوريا، والكرياتينين، ومستويات أقل ذات دلالة إحصائية في الكوليسترول عالي الكثافة . (HDL) كما سجَّلت مجموعة السكري دون اعتلال كلوي (G2) انخفاضًا ذا دلالة إحصائية في مستوى الأنسولين مقارنةً بـ (G1) .أما بين مجموعتي مرضى السكري ((G2 و (G3) كانت مستويات الكوليسترول الكلي، والدهون الثلاثية، واليوريا أعلى بشكل ذي دلالة إحصائية في مجموعة اعتلال الكلية (P≤0.05) (G3)، بينما لم تُظهِر مقارنة سكر الدم الصائم (FBG)، والهيموغلوبين السكري (HbA1C)، والكرياتينين، والكوليسترول عالي الكثافة (HDL)، والأنسولين فروقًا ذات دلالة إحصائية (P>0.05). ارتفع مستوى بروتين الديكورين في مصل الدم بشكل ذي دلالة إحصائية في مجموعة السكري دون اعتلال كلوي (G2) مقارنةً بالمجموعة الضابطة (G1) ، كما أظهر زيادة كبيرة ذات دلالة إحصائية في مجموعة اعتلال الكلية (G3) مقارنةً بمجموعة السكري دون اعتلال كلوي (G2) . أخيرا ترتبط المستويات المرتفعة لبروتين الديكورين بمرض السكري من النوع الثاني (T2DM)، وتزداد هذه المستويات بشكل أكبر مع الإصابة باعتلال الكلية. يشير هذا إلى دور هام لبروتين الديكورين في تطور اعتلال الكلية السكري. قد يصلح بروتين الديكورين لأن يكون علامة حيوية قيِّمة للتنبؤ بتقدم مرض الكلى السكري.

الكلمات المفتاحية : اعْتِلالُ الكُلَى السُّكَّرِيّ ، ديكورين ، مَرَضُ الكُلَى المُزْمِن ، المَعايِيرُ الكِيمْيَائِيَّةُ الحَيَوِيَّة ، الانسولين .

Introduction:

Diabetes mellitus (type 2) is a chronic illness that causes by hyperglycemia arising from either an insulin shortage, decreased insulin activity, or both [1]. By 2035, diabetes is expected to affect 600 million people, accounting for more than one in every 10 individuals [2]. End-stage kidney disease (ESKD) is a common term used to characterize persons who are in the final stages of chronic kidney disease (CKD) and are getting dialysis treatment or a kidney transplant for treatments [3]. Type 2 diabetes accounts for approximately 95% of most populations. The diabetes epidemic has led to an increase in diabetic nephropathy "DN" A distinctive group of anatomical and functional kidney abnormalities in diabetic patients is referred to as diabetic nephropathy "DN [4] . The functional changes include systemic hypertension, proteinuria, early rise in glomerular filtration rate with intraglomerular hypertension, and eventually demise of renal function [5], According to Mogensen *et al.*, DN can be divided into five distinct stages. 1) Early hypertrophy stage: defined by an increase in GFR and renal plasma flow; 2) Silent stage: related to mild morphological changes such as glomerular hypertrophy, thickening of the glomerular basement membrane, mesangial formation, and tubulointerstitial expansion; 3) Incipient disease "DN": identified through microalbuminuria with probable hypertension onset; 4) Evident disease "DN": defined by dipstick-positive proteinuria; and 5) End-stage renal disease (ESRD) with uremia [6]. Small vessel disease is the first step in the developments of diabetic nephropathy, which includes intricate processes such protein glycosylation, cytokine release (such as TGF-beta), mesangial matrix deposition, and changed glomerular hemodynamics [7]. Diffuse or nodular intercapillary glomerulosclerosis is one of the main lesions; Kimmelstiel-Wilson lesions are particularly noteworthy. In addition, there is tubular atrophy, arteriosclerosis, hyalinosis of the arterioles, and interstitial fibrosis. Expanding mesangial matrix is specifically linked to the development of end-stage renal disease [8]. this is the main reason why chronic kidney ac-

crues in industrialized countries [9, 10]. Diabetic nephropathy "DN", a severe microvascular consequence of diabetes mellitus (DM), is one of the main causes of CKD and often leads for end-stage renal disease (ESRD) [11]. DN affects approximately thirty percent of patients with type 1 diabetes and forty percent of those with type 2 [12]. Diabetics incidence is quickly increasing internationally, particularly in poorer nations [13]. As diabetes becomes more common, the prevalence of DN is expected to rise until therapeutic preventative strategies improve [14]. The etiology of DN growing and progressing is complicated and multifaceted, contained several routes and intermediaries [15]. Clinically, DN is defined as increasing renal damage evidenced by chronic albuminuria and decrease of glomerular filtration rate (GFR), hypertension, and excess death owing to ESRD or cardiovascular problems [16] as well as higher cardiovascular and total mortality in patients receiving hemodialysis [17]. Diabetic retinopathy is diagnosed by combining estimated GFR (eGFR) and albuminuria with clinical features of DM, including disease progression and the presence of diabetic retinopathy [18]. DN is defined as a prolonged urine albumin to creatinine ratio of ≥30 mg/g and/or a sustained fall in eGFR below 60 mL/min/1.73 m2 [19, 20] The early diagnosis, close observation, and effective treatment of diabetic nephropathy depend on these factors [21].

Decorin (DCN) belongs to the small leucine-rich proteoglycan SLRP gene family, including core proteins with leucine-rich repeats. Soluble decorin not only regulates collagen fibrillogenesis and TGF-b activity, additionally inhibits pan-receptor tyrosine kinases (RTKs), TGF-1 increases the excretion of glucose, albumin, electrolytes, and water in urine, leading to glomerulosclerosis, interstitial fibrosis, and reduced GFR in DM [22]. Decorin connects to many RTKs, including EGFR, HER2, HGFR/Met, VEGFR2, TLR, and IGFR [23, 24]. DCN regulates cellular processes via attaching to ECM molecules or cell surface receptors, including TGF-b, EGFR, IGF-1R, and VEGFR2. DCN has several positive benefits, including reducing fibrogenesis, inflammation, tumor development,

and metastatic dissemination [25]. SLRPs, an 18-gene family, are a specific groups of proteoglycans with many functions in the extracellular matrix (ECM) [26, 27]. A recent study demonstrated that diabetic nephropathy was ameliorated by decorin [28]. Research suggests that inhibiting apoptosis and fibrosis can protect against diabetic nephropathy [29]. There are several investigations have shown by C. H. Park and T.-H noted that decorin insufficiency worsens diabetic nephropathy in a mouse model [30]. **Aim of this study** is investigate the evaluated serum decorin levels and other biochemical parameters in diabetic nephropathy patients to assess potential links with disease development in type 2 diabetes mellitus (T2DM).

Patients and Methods:

The one hundred fifty (150) individuals in the research study with an average age (35-50) years were had been separated onto three different groups: (G1), that contained of fifty healthy peoples who declared as a healthy control groups ; (G2) , which involved about A fifty individuals who suffer from type 2 diabetes mellitus (T2DM) who were included in the second group(G2). Group3, which consisted of fifty people who have been diagnosed patients for diabetic without nephropathy as of Groups3(G3). A collection of blood samples takes happen between the months from December 14, 2023, and May 22, 2024. The researchers started the methods of calculating a person's body mass index(BMI). Everyone who participated had a sample of their venous blood that measured five milliliters obtained from them. To obtain an accurate estimate of the amount of HbA1C, one milliliter of whole blood was required. To analyze the levels of Decorin and insulin, an ELISA test was performed using kits obtained from Mybiosource in the United States. The serum concentrations of FBG, TC, TG, HDL, urea, and creatinine were determined using manual techniques.

The statistical analysis was performed using the Statistical Packages for the Social Sciences, version 21 (SPSS-21) application. If the P value was equal to or less than 0.05, it was considered statistically significant. Pearson's correlation was used to establish a correlation between two

quantitative variables, and the t-test was used to determine whether the connection was significant. Three distinct groups evaluated the Receiver Operating Characteristic (ROC) curves for Decorin.

Results & discussions :

The results of the FBG, HbA1c, insulin, TC, TG, HDL, urea, creatinine and the Decorin tests are displayed in Table (1). Based on the data that was given the levels of FBS, HbA1C and creatinine levels for G2 and G3 showed significant increase (P≤0.05) compared to G1, since there are non- significant rising (P>0.05) was found between G2 and G3. The Total cholesterol, triglycerides and B.urea levels in G2 and G3 showed significant rising (P≤0.05) compared to G1, and there are significant increase (P>0.05) was found between G2 and G3. The HDL levels in G2 and G3 had significantly lower (P≤0.05) compared to G1, while there are non- significant rising (P>0.05) was found between G2 and G3. Insulin levels in G2 decreased significantly (P≤0.05) compared to G1, whereas no significant increase (P>0.05) was observed between G1 and G3. Decorin levels showed a important rise (P≤0.05) in G2 compared to G1. Table (1) shows the level of Human Decorin (DCN) among the control group "G1", , type 2 diabetes mellitus individuals T2DM "G2" and nephropathy diabetics "G3" . The results showed a significant decrease in DCN level in both G1 and G2 (288.6±49.96 Mg/dl and 184.92±62.56 Mg/dl respectively) in comparison with healthy control group (355.1±75.5 Mg/dl). This decrease was significantly higher in G2 when compared with G1. Decorin is a tiny proteoglycan that affects cell signaling, collagen fibrillogenesis, and the organization of extracellular matrix [31]. Changes in DCN levels can affect the structure and function of tissues, which can lead to the pathophysiology of illness [32]. A reduction in DCN levels could be a sign of extracellular matrix remodeling or disintegration, which is frequently seen in a number of disease conditions, such as renal and diabetes [32]. Nephropathy may cause fibrosis and inflammation that affect the nature of the extracellular matrix, changing the amounts of DCN. When weighed against the more widespread conse-

quences of diabetes, the magnitude of this alteration might be smaller [33]. As seen in G2, type 2 diabetes can result in extensive changes to the extracellular matrix components an outcome of oxidative stress, inflammation, and persistent hyperglycemia. Any of these changes can produce more notable reductions in DCN levels. The impact of illness on extracellular matrix components is shown by the decrease in DCN levels in both patient groups. The more marked decline in T2DM patients indicates that more research is necessary to understand how diabetes impacts matrix remodeling and whether treatments can lessen these effects.

Table 1: Mean & SD for FBS, Hb1AC, insulin, TC, TG, HDL, urea, creatinine and Decorin levels in G1& G2 .

Parameters	Means ± SD			
	G1 (n=50)	G2 (n=50)	P value	P value (G2&G3)
FBS	86.9±4.58	194.46±39.28	<0.001	0.75
HbA1C %	5.3±0.36	8.47±1.37	0.001>	0.213
Insulin (mg/dl)	18.71±4.66	14.93±1.57	<0.001	0.005
TC (mg/dl)	180.86±8.08	205.96±33.4	<0.001	0.016
TG (mg/dl)	112.33±17.16	181.53±34.83	<0.001	0.001
HDL (mg/dl)	48.933±2.92	44.33±2.72	0.001>	0.124
B.urea (mg/dl)	30.43±3.66	36.66±7.8	0.001>	>0.001
S.creatinine (mg/dl)	0.7±0.07	1.19±1.72	0.12	0.84
Decorin (mg/dl)	355.1±75.5	184.92±62.56	0.001>	0.001>

G1: Healthy Control, G2: T2DM diabetes,
G3: T2DM with nephropathy, N.S: Non-significant: p>0.05

Correlation studies of Decorin with other parameters.

The findings of these study on the relationship among Decorin and parameters are shown in Table 2 & 3 for G_1, G_2, also G_3.

Table 2: The Relationship between Serum Decorin and other Variables studied in patients with Type 2 Diabetic (G2)

	parameters	r	p
Decorin	FBG(mg/dl)	0.218	0.307 (N.S)
	HbA1C %	-0.019	0.93 (N.S)
	Insulin(mg/dl)	0.043	0.843 (N.S)
	TC(mg/dl)	-0.012	0.957 (N.S)
	TG(mg/dl)	-0.07	0.747 (N.S)
	HDL(mg/dl)	-0.065	0.763 (N.S)
	B.urea	0.019	0.929 (N.S)
	s.creatinine	0.108	0.615 (N.S)

Figure 1: correlation Relation of Decorin for G2

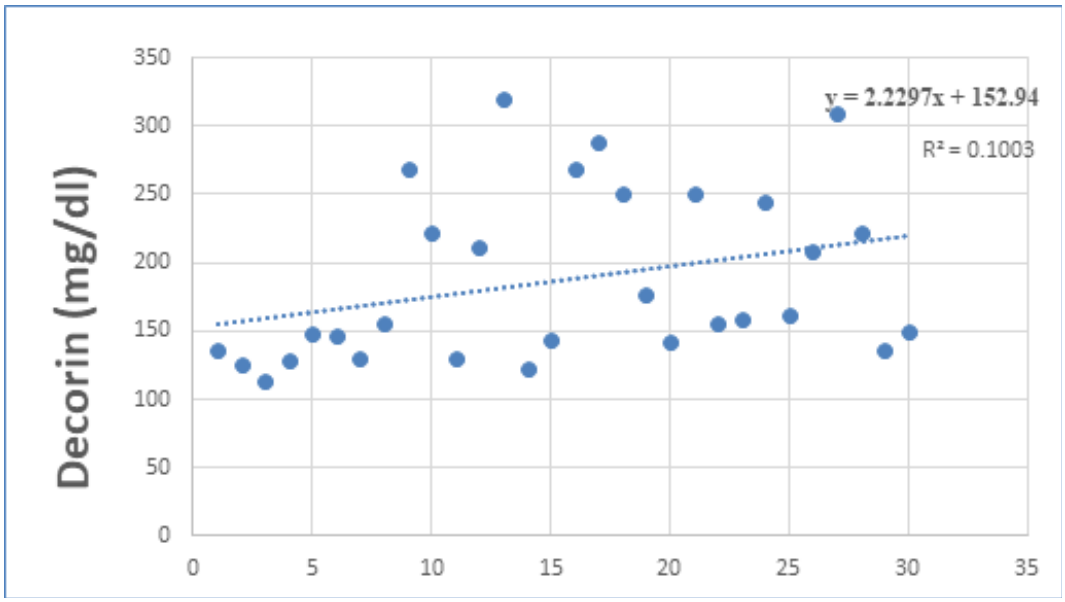

Table 3: The Relationship between Serum Decorin and other Variables studied in patients of Type 2 Diabetic with nephropathy (G3)

	parameters	r	p
Decorin	FBG(mg/dl)	-0.167	0.379 (N.S)
	HbA1C %	0.181	0.339 (N.S)
	Insulin (mg/dl)	0.026	0.891 (N.S)
	TC (mg/dl)	0.345	0.062 (N.S)
	TG (mg/dl)	0.352	0.056 (N.S)
	HDL (mg/dl)	-0.007	0.969 (N.S)
	B.urea	0.285	0.127 (N.S)
	s.creatinine	-0.049	0.797 (N.S)

Roc curve for serum Decorin :

ROC for Decorin in T2DM

The ROC curve analysis for DCN across two distinct groups reveals an area AUC value of 0.974. This AUC value is statistically significant at as indicated by the p-value <0.001 (Figure 2). The optimal cut-off value for DCN has been determined to be ≤269.3, having a sensitivity of 91.67% as well as specificity of 100% (Figure 2) (Table 4). Overall, DCN is a highly effective biomarker for distinguishing between the two groups, with excellent predictive accuracy.

Table4: Difference between sensitivity and specificity for Decorin in T2DM (G2) & Diabetic Nephropathy (G3).

Parameter	Sensitivity	Specificity	AUC	P-value	Cut off
Decorin in T2DM	91.67%	100.00%	0.974	<0.0001	≤269.3
Decorin in Nephropathy	100.00%	50.00%	0.750	<0.0001	>248

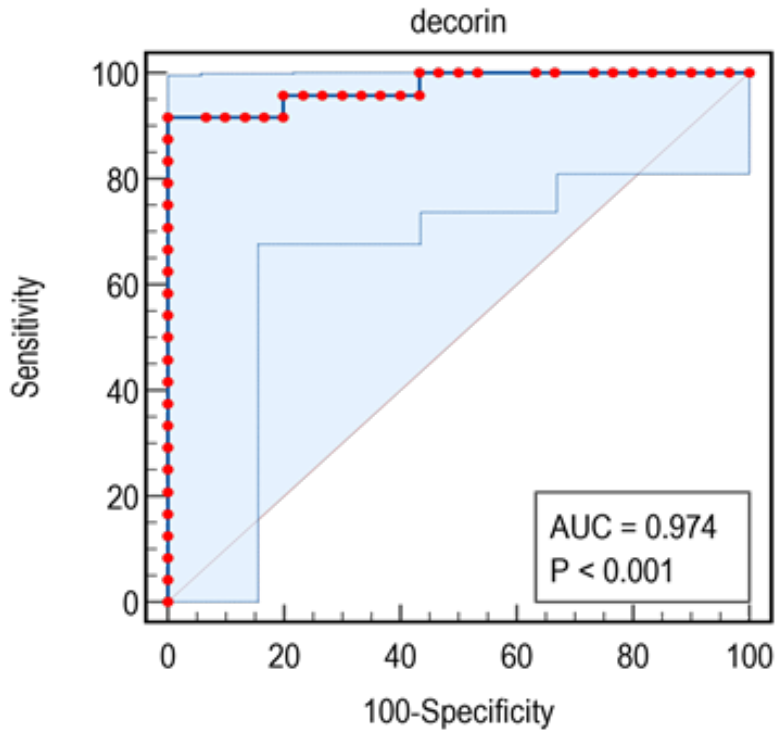

Figure 2 : ROC diagnosis for Decorin in T2DM (G2)

ROC study for Decorin for NP Control and Patients Group:

The Receiver Operating Characteristic (ROC) curve testing for decorin across two distinct groups (control group and NP patients' group) reveals an area under the curve (AUC) value about 0.750. This AUC value is statistically significant as indicated by the p-value <0.001 (Figure 3). The optimal cut-off value for decorin is founded to be >248, and having a sensitivity of 100% and a specificity of 50% (Figure 3). The results indicate that decorin is a moderately effective marker for distinguishing between the control and NP patients' groups. The statistically significant cut-off value of >248 provides perfect sensitivity but lower specificity, making it highly effective for identifying positive cases but less reliable for excluding negative ones.

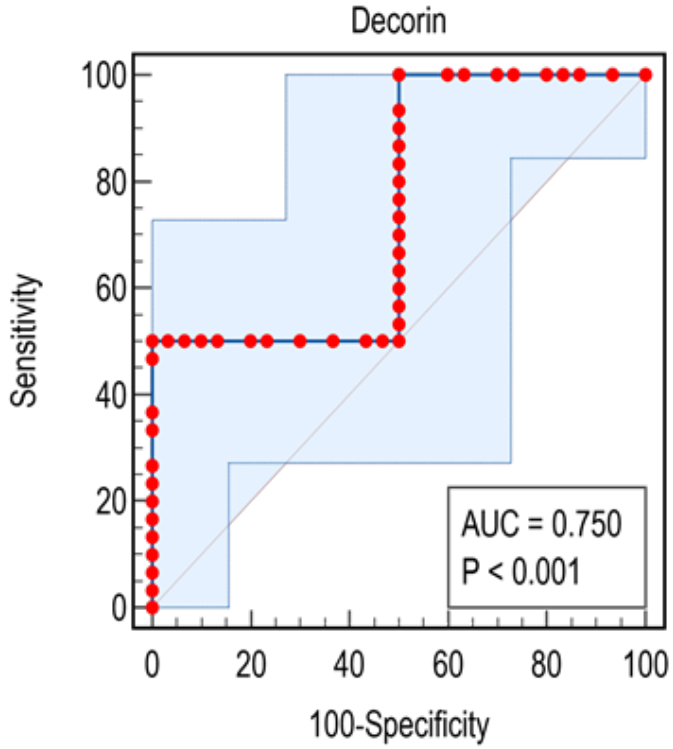

Figure 3: ROC diagnosis for Decorin in NP

Conclusions:

Current study shown that function markers (Decorin) can be utilized to forecast the progression of Diabetic Nephropathy Disease in peoples having Type2 diabetes.

Decorin may be useful in monitoring and early prediction of kidney problems in diabetic patients with Diabetic kidney Disease.

Author contributions:

Amenh Muhammed Abdul Rahman: the conceptualization, Collecting data, Formal analyses, Funding purchase, Resources, Methods, Project management, Writing-Review, and Editing. **Nawal Mohammed Jawad Al-shammaa**: Conceptualization, Collecting data, Formal analyses, Funding acquisition, Resources, Methods, Project management, Supervision, Writing-Review, and Editing.

Authors' declaration:

There is no conflict of concern .

We thus attest that we own every Figure and Table in this manuscript .

Acknowledgments:

I would like to express my deepest gratitude to the **University of Baghdad, college of education for pure science Ibn-AlHaithem, chemistry department & Al-Iraqia University, college of medicine, pharmacology department, Baghdad, Iraq**. For providing me with the academic foundation and resources necessary to pursue my research and studies. the support and guidance from faculty and staff have been invaluable in shaping my academic journey.

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