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Table 1. Main characteristics of the included studies

Author	Year	Total sample size	Study design	Country	Mean age (case/control)	Cases	Controls	Diabetes/MetS comorbidities	Body fluid	Quality scores
Afify et al.	2009	80	Case-control	Egypt	31.3 ± 15.2, 32.4 ± 18.8	CHD	Healthy infants and children	Without	Serum	Low
Chen et al.	2014	200	Cohort	China	67.1 ± 19.5, 69.6 ± 23.8	CHF	Healthy subjects	Without	Plasma	High
GHAZI#a et al.	2019	75	Case-control	Iraq	47.79 ± 8.34, 57.68 ± 7.01	MI with DM	Healthy subjects	With	Serum	High
GHAZI#b et al.	2019	75	Case-control	Iraq	47.79 ± 8.34, 54.48 ± 9.41	MI without DM	Healthy subjects	Without	Serum	High
Hamed et al.	2012	84	Case-control	Egypt	20.3 ± 0.21, 24.3 ± 0.41	AMI	Healthy subjects	With	Serum	High
Kandil et al.	2009	58	Case-control	Egypt	15.67 ± 7.81, 13.23 ± 8.38	CHD	Healthy control children	Without	Serum	Low
Kilic et al.	2017	61	Case-control	Turkey	49.5 ± 12.2, 50.5 ± 11.0	IHD	Healthy subjects	Without	Serum	High
Lund et al.	2009	19	Cross-	New	42 ± 14,	HF	Healthy	With	Plasm	High

			sectional	York	52 ± 16		subjects		a	
Matsumoto #a et al.	2013	15	Case-control	Japan	66 ± 5, 66 ± 6	SAP	Control without significant coronary artery stenosis	With	Serum	High
Matsumoto #b et al.	2013	14	Case-control	Japan	66 ± 5, 64 ± 5	UAP	Control without significant coronary artery stenosis	With	Serum	High
Matsumoto #c et al.	2013	18	Case-control	Japan	66 ± 6, 67 ± 10	AMI	Control without significant coronary artery stenosis	With	Serum	High
Nagaya et al.	2001	86	Case-control	Japan	57 + 13.416,	CHF	Healthy subjects	Without	Plasma	High
Özcan et al.	2015	83	Case-control	Turkey	67 ± 10, 67.38 ± 7.57	ADHF	Healthy subjects	With	Serum	High
Shahramian et al.	2013	64	Cohort	Iran	3.22 ± 3.49, 3.3 ± 4.27	CHD	Healthy subjects	Without	Serum	High
Xin et al.	2009	80	Case-control	China	63.9 ± 2.1	CHF	Healthy	Without	Plasm	High

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							subjects		a	
Yilmaz et al.	2007	93	Case-control	Turkey	2.59 ± 1.258, 2.41 ± 1.36	CHD	Healthy children	Without	Serum	High
Zabarovskaja et al.	2014	24	Cross-sectional	Sweden	24 ± 3.7, 57 ± 10.37	HF	Healthy subjects	With	Plasma	High
Zhang#1 et al.	2011	216	Case-control	China	74.6 ± 9.5, 76.2 ± 9.6	CAD	Healthy subjects	Without	plasma	High
Zhang#2a et al.	2012	84	Case-control	China	NR	ACS	Control without diabetes	With	Plasma	High
Zhang#2b et al.	2012	95	Case-control	China	NR	SAP	Control without diabetes	With	Plasma	High

Abbreviations: CAD: Coronary artery disease; CVD: Cardiovascular disease; CHD: Congenital heart disease; CHF: Congestive heart failure; CAE: Coronary artery ectasia; HF: Heart failure; AF: Atrial fibrillation; MI: Myocardial infarction; DM: Diabetes mellitus; PSVT: Paroxysmal supraventricular tachycardia; AMI: Acute myocardial infarction; IHD: Ischemic heart disease; HD: Hemodialysis; SAP: Stable angina pectoris; UAP: Unstable angina pectoris; IDC: Idiopathic dilated cardiomyopathy; ADHF: Acute decompensated heart failure; HHD: Hypertensive heart disease; BAV: Bicuspid aortic valve; ERAF: Early recurrence of atrial fibrillation; ACS: Acute coronary syndrome; STEMI: ST-elevation myocardial infarction; Non-STEMI: Non-ST-elevation myocardial infarction; NR: Not recorded; MetS: Metabolic syndrome

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Table 2. Subgroup analysis results

Outcomes	Subgroups		No. studies	SMD	95% CI	I^2 (%)
Ghrelin	Total		20	-0.61	-1.38, 0.16	96.9
	Study design	Case-control	16	-0.92	-1.90, 0.07	97.4
		Cohort	2	-0.39	-1.28, 0.49	87.6
		Cross-sectional	2	0.71	-0.02, 1.43	0.0
	Diabetes/MetS comorbidities	With	10	-2.60	-4.17, -1.02	96.8
		Without	10	0.78	-0.02, 1.59	96.3
	Body fluid	Plasma	8	-0.54	-1.40, 0.31	95.2
		Serum	12	-0.94	-2.23, 0.35	97.4
	Heart diseases	CAD	9	-3.14	-4.62, -1.66	97.3
		Other diseases	11	1.02	0.27, 1.77	94.7
	Continent	Africa	3	-5.75	-10.80, -0.69	98.9
		Europe	4	1.53	0.25, 2.81	93.5
		America	1	0.86	-0.12, 1.84	-
		Asia	12	-0.99	-1.68, -0.30	94.3
Ghrelin/TC ratio	Total		11	-1.02	-1.74, -0.29	94.5
	Study design	Case-control	10	-1.17	-2.05, -0.28	94.9
		Cohort	1	-0.07	-0.38, 0.24	-
	Diabetes/MetS comorbidities	With	5	-2.33	-5.11, 0.45	96.2
		Without	6	-0.20	-0.57, 0.17	94.5
	Body fluid	Plasma	4	-0.02	-0.20, 0.16	0.0
		Serum	7	-1.79	-3.28, -0.30	95.7
	Heart diseases	CAD	7	-1.79	-3.19, -0.40	96.4
		Other diseases	4	-0.02	-0.24, 0.21	0.0
	Continent	Africa	1	-9.27	-10.79, -7.75	-
		Europe	1	0.09	-0.42, 0.59	-
		Asia	9	-0.44	-0.89, 0.01	82.4

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Ghrelin/HDL-c ratio	Total		11	-0.43	-0.96, 0.10	90.7
	Study design	Case-control	10	-0.49	-1.12, 0.14	91.5
		Cohort	1	-1.01	-0.32, 0.30	-
	Diabetes/MetS comorbidities	With	6	-0.87	-2.32, 0.58	94.9
		Without	5	-0.00	-0.17, 0.17	0.0
	Body fluid	Plasma	3	-0.00	-0.19, 0.19	0.0
		Serum	8	-0.64	-1.56, 0.28	93.2
	Heart diseases	CAD	7	-0.74	-1.76, 0.27	94.2
		Other diseases	4	0.00	-0.21, 0.21	0.0
	Continent	Africa	1	-4.81	-5.71, -3.91	-
		Europe	2	0.02	-0.32, 0.35	0.0
		Asia	8	-0.02	-0.18, 0.15	0.0
Ghrelin/LDL-c ratio	Total		11	-0.09	-0.23, 0.05	0.0
	Study design	Case-control	10	-0.11	-0.27, 0.05	0.0
		Cohort	1	-0.03	-0.34, 0.28	-
	Diabetes/MetS comorbidities	With	6	-0.17	-0.44, 0.09	0.0
		Without	5	-0.06	-0.23, 0.11	0.0
	Body fluid	Plasma	3	-0.01	-0.20, 0.18	0.0
		Serum	8	-0.19	-0.40, 0.02	0.0
	Heart diseases	CAD	7	-0.17	-0.37, 0.03	4.7
		Other diseases	4	-0.01	-0.22, 0.20	0.0
	Continent	Africa	1	-0.00	-0.51, 0.50	-
		Europe	2	0.00	-0.33, 0.33	0.0
		Asia	8	-0.12	-0.29, 0.04	0.0
Ghrelin/TG ratio	Total		12	-0.55	-1.16, 0.07	93.1
	Study design	Case-control	11	-0.71	-1.45, 0.02	93.7
		Cohort	1	-0.01	-0.32, 0.30	-
	Diabetes/MetS comorbidities	With	6	-2.91	-4.99, -0.83	96.8
		Without	6	-0.03	-0.19, 0.13	93.1
	Body fluid	Plasma	4	-0.00	-0.18, 0.18	0.0

		Serum	8	-1.55	-2.78, -0.32	95.6
	Heart diseases	CAD	7	-1.86	-3.21, -0.50	96.2
		Other diseases	5	0.00	-0.19, 0.20	0.0
	Continent	Africa	1	-26.07	-30.13, -22.00	-
		Europe	2	0.02	-0.31, 0.36	0.0
		Asia	9	-0.07	-0.23, 0.09	0.0

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Met-regression results

Suppl Fig. Fb (Ghrelin)

Funnel plot with pseudo 95% confidence limits