scientific reports

OPEN

Prevalence of metabolic syndrome and its components according to altitude levels: a systematic review and meta-analysis

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Metabolic syndrome has a multifactorial origin; however, epidemiological data correspond to populations located at sea level. It has been reported that the altitude can affected the prevalence due to physiological changes. The aim of this study is to show the global prevalence of metabolic syndrome at altitude and its components. We use four databases, all studies published up to November 2023. The prevalences from studies were meta-analyzed using a random-effects model. To assess sources of heterogeneity, subgroup analyses were performed. We included 28 studies. The number of participants was 29 195. The prevalence of metabolic syndrome was 30.3% (95% CI 22.8–38.4%). According to the altitude level, at 1500–2500 was 36.5%, 2500–3500 (21.8%), and > 3500 (30.9%), also it was higher in women (35.5%) that men (26.8%). It was observed that there is an inverse relationship between higher altitude and the prevalence of metabolic syndrome. Among its components, abdominal obesity and low HDL were present in more than 40.0%, while high blood pressure, high triglycerides and impaired glucose were present in less than 30.0%. We recommend that our results be considered for future research in populations living at altitude since they have different characteristics from populations at sea level.

Keywords Metabolic syndrome, Altitude, Prevalence, Public health, Meta-analysis

Metabolic syndrome (MetS) is defined as the concomitant presence of several risk factors such as atherogenic adiposity, dyslipidemia, elevated blood pressure and/or insulin resistance, which in turn correspond to their components[1,2]. The situation predisposes to the development of cardiovascular disease and type 2 diabetes mellitus[3]. MetS has received increased attention due to its high prevalence in the general population[4]. In addition, it has been demonstrated that this pathology has continued to grow over the last two decades[5,6], with prevalences ranging from 27.4 to 39.0%[7–9].

MetS has a multifactorial origin, where lifestyle, geographic locations, and ethnic groups are added[1]; however, epidemiological data correspond mostly to populations located at sea level, without considering those living at altitudes above 1 500 meters above sea level (m.a.s.l). It has been reported that in this environment, the prevalence of MetS can be affected[10] due to physiological changes that occur at altitudes above 1 500 m.a.s.l[11], where approximately 500 million people live[12]. It has been found that people living at altitude tend to maintain adequate body weight and low insulin resistance, but high blood pressure and unfavorable serum lipid levels conditions may affect the prevalence of MetS[12]. However, reports in the literature diverge in explaining these findings. Among the studies reporting MetS prevalences, one study showed a higher prevalence of MetS at altitude compared to sea level (59.0% vs. 21.0%)[13]. Similarly, each of the MetS components reports variations

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in reported prevalences, such as high blood pressure, which is higher in Tibetan adults compared to global estimates (31.4% vs. 22.0%)[14]. As is the prevalence of obesity, which is higher in people living at altitudes (19.7% vs. 9.7%)[15]. Results contrary to those reported in large Latin America studies such as ENSANUT—ECU where the components of MetS, except hypertriglyceridemia, were less frequent in high altitude areas (29.5% vs. 34.1%)[16]. Similarly, the CRONICAS cohort study found that the frequency of obesity is lower at higher altitudes (21.6% vs. 88.4%)[17]. These studies show the controversy regarding the prevalence of MetS at different altitude levels and its components.

Systematic reviews (SR) and meta-analyses have identified a pooled prevalence of MetS of 12.0% in rural areas vs. 22.5% in urban areas[18]. Similarly, one SR estimated an overall prevalence of MetS between 12.5% and 31.4%[19]. However, in both studies, the prevalence was not differentiated by altitude level, and these different reported prevalences may be explained by the physiological changes that occur at different altitude levels (intermediate, high, very high, and extreme)[11] and by altitude residence regions[20] that diverge from each other, even at the genetic level[21]. In addition, research on metabolic diseases in altitude regions is scarce[22,23]. The prevalence of MetS is modified by smoking, alcohol consumption, red meat intake[24], and hiking activities[25], demonstrating that the prevalence of MetS may differ according to geographical factors, nutritional patterns, and physical activity of the population. Therefore, the present study aims to demonstrate through a systematic review and meta-analysis the global prevalence of MetS, each of its diagnostic criteria, the differences between age group, type of resident, level of altitude, continent, type of definition and type of population since they represent variables not evaluated in other studies.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines Supplementary Material 1[26]. The protocol was registered with PROSPERO, number CRD42021291083.

Eligibility criteria

We included cross-sectional and cohort studies that presented information on the prevalence of MetS in people living at high altitudes (resident or native people) worldwide. Among the inclusion criteria, we considered (1) studies with a inhabitants population at an altitude higher than 1 500 m.a.s.l., considering that, according to the literature, physiological and systemic changes occur after this limit[11]; (2) that each of the studies reports the use of MetS criteria as the International Diabetes Federation's (IDF)[27], National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III)[28] and others[29]; (3) the definition of settlers as resident (defined as a person who leaves his or her city of birth to settle in another place and has a period of stay of more than 12 months in the altitude) and native (defined as a person who has been born and resides in the altitude).

Exclusion criteria included manuscripts that were not available in full text, incorrect study design (referring to editorials, comments, opinions, and narrative reviews that did not present the necessary data for analysis), and studies with incorrect populations (referring to studies with a population that does not belong to altitude regions).

Bibliographic search and selection of studies

A systematic search was performed in four databases: Web of Science (WoS), Scopus, PubMed and Embase. About the search time, all studies published up to November 2023 were considered. No language restrictions were applied. The complete search of each database is available in Supplementary Material 2. The bibliographic references of the included studies were also reviewed for potentially eligible studies.

The studies were exported to the Rayyan Software program[30], where duplicates were manually removed. Subsequently, five authors (PGE—FSA—MRCM—JCB—ADCS—JTF) independently reviewed the articles by titles and abstracts to identify potentially relevant articles for inclusion. A third author (JPZV) resolved discrepancies at this stage. The chosen studies proceeded to full-text review where they participated (PGE—FSA—MRCM—JCB—ADCS—JTF). Likewise, this process was performed independently, and discrepancies were resolved by a third author (JPZV). At this point, the excluded studies with their reasons for exclusion can be seen in Supplementary Material 3.

Data extraction and assessment of methodological quality

Four authors (PGE—FSA—JCB—JTF) independently extracted the following data of interest using a Microsoft Excel sheet: author, year of publication, study design, country, sample size, age, sex, type of resident, altitude level, the prevalence of MetS globally and the prevalences of each component, and whether the studies reported by sex (male and female). Discrepancies were resolved by two authors (FSA and MRCM).

Likewise, four authors (JPZV—PGE—JCB—ADCS) independently assessed the methodological quality of prevalence studies using the Joanna Briggs Institute Critical Appraisal Tool[31]. Another author (JPZV) resolved discrepancies in this process. This scale has 9 items with possible answers of "Yes" (1 point), "No" (0 point) and "Unclear" (0 point). The quality score presented in Supplementary Material 4 was considered as one point for "Yes" and zero points for "No" and "Unclear". In addition, we categorized the risk of bias into high, moderate, and low according to scores of 0 to 3, 4 to 6, and 7 to 9, respectively. Sensitivity analysis was not performed because all included studies were at low risk of bias. Supplementary Material 4.

Statistical analysis

To assess the proportion of metabolic syndrome, we decided to calculate pooled proportions using mixed-effects models for sample differences in each study with 95% confidence intervals. The Freeman-Turkey Double transformation was used to stabilize variances. In relation to studies with two or more groups, to the analyzes we chose the group with more participants. We decided not to use Egger's test or funnel plots, as their usefulness for assessing publication bias in the meta-analysis of prevalence is unclear and the results may reflect selection bias. Six subgroup analyses were prespecified according to the available data: type of resident (rural and urban), type of population (native and resident), continent (Asia and America), altitude levels (1500 to 2500, 2500 to 3500 and > 3500 m.a.s.l), type of criteria definition used according to the guideline used for the diagnosis of MetS, age group (<55 years and >= 55 years) and sex (men and women), at this point, we believe that at least two studies should have the necessary information. Assessment of heterogeneity included the Cochrane Q p-value (< 0.10 denotes statistical significance) along with the I2 statistics. When the percentages of I2 value s were 0–40, 30–60, 50–90 and 75–100, they represented possibilities of minor, moderate, substantial and significance heterogeneity, respectively. Statistical significance of the summary estimates was determined with a *p*-value <0.05. To assess heterogeneity and its sources, we used the I^2 test and performed subgroup analyses according to population: sex, country, risk of bias, and altitude. Additionally, meta-regression was carried out to establish whether any of the characteristics of the studies were a source of heterogeneity and the residual heterogeneity percentage. The statistical program Stata v.17 (StataCorp, College Station, TX, USA) was used for all statistical analyses.

Results

Selection and inclusion of studies

After eliminating duplicates, 780 studies remained to be evaluated by title and abstract. A total of 56 studies were evaluated in full text to assess their eligibility, from which 23 were selected, and another five were selected from other sources. Twenty-eight studies were included in the review (Fig. 1).

Characteristics of studies evaluating the prevalence of metabolic syndrome and its components at altitude (Table 1*)*

Of the 28 studies, only one was of cohort design[32]. The number of participants in all studies was 29,195 and ranged from 18 to 80 years. The altitude level of residence of the study participants ranged from 1500 to 4500 m.a.s.l. The countries where the studies were carried out were: Peru[32–39], China[12,40–43], Ecuador[16,38,44–47], Bolivia[48], Mexico[49–53], and India[54–56]. Some studies evaluated the overall prevalence and components of MetS[12,16,32,34–38,40,44,47,55–57]. On the other hand, only eight studies specified that their populations were natives[12,33,34,39,41,42,44,51,55,56,58]. About the guideline used for the diagnosis of MetS, nine studies used the IDF[16,34,35,38,45–47,56,58], nine used the NCEP-ATP III[33,34,36,42–44,47,50–52,56,57,59], and others used other instruments[12,37,39,41,46,48,49,54] (Table 1).

Prevalence of metabolic syndrome according each parameter

Twenty-eight studies were synthesized for meta-analysis of metabolic syndrome (MetS) prevalence at altitude (> 1500 m.a.s.l). The pooled prevalence of MetS was 30.3% (95% CI 22.8–38.4%), with significant heterogeneity (I^2: 99.5%) among studies. In men, the pooled prevalence of MetS was 26.8% (95% CI 18.5–36.0 %; I^2: 98.9%), in women was 35.5% (95% CI 24.8–47.01%; I^2: 99.5%), both synthesized from 21 studies (Fig. 2).

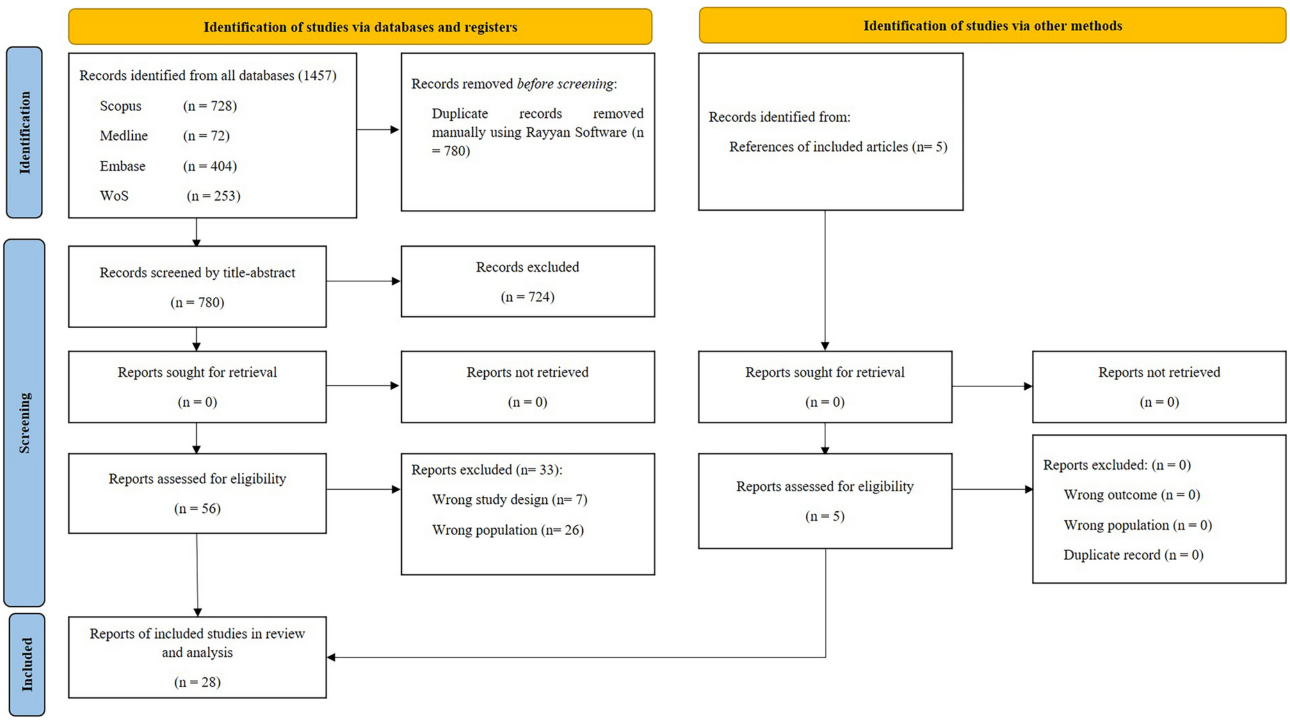

Fig. 1. Flow diagram summarizing the process of literature search and selection

Author	Country	Altitude level	Sample size	Type of inhabitant	General characteristics			Continent	Definition of MetS	Prevalence of MetS (%)						Quality score (Max. 9)
					Age (mean ± SD years or median (IQR))	Female (%)	Urban (%)			Total	Abdominal perimeter (%)	High level of trigliceridos (%)	Alteration of blood glucose (%)	Blood pressure (%)	Low HDL (%)	
Baldeón et al.[44]	Ecuador	2800	1997	N	65.9 (5.3)	72.06	100	America	LAC-HTA-D_MS	43.42	89.41		10.35			Low risk
Baracco et al.[33]	Peru	4100	99	N	67.4 (5.8)	63.64	0	America	NCEP-ATP III	24.24	40.40	56.56	14.14	18.18	30.3	Low risk
Chimbo-Yunga et al.,[47]	Ecuador	2560	387	R	72.8 (7.5)	25.02	100	America	NCEP-ATP III	59.95	47.30	38.20	15.80	59.40	74.7	Low risk
Díaz-Cisneros et al.[50]	Mexico	2045	477	R	20 - 60	56.00	NM	America	NCEP-ATP III	29.55						Low risk
Echavarría-Pinto et al.,[51]	Mexico	1920	73	N	20 - 39	57.53	NM	America	NCEP-ATP III	45.20						Low risk
Pérez-Galarza et al.,[16]	Ecuador	> 1500	4127	R		64.6	NM	America	IDF	29.54	18.66	9.33	3.12	5.23	17.28	Low risk
González-Chávez et al.,[59]	Mexico	2240	189	R	38.6 (13.2)	66.00	NM	America	NCEP-ATP III. IDF. OMS	41.74						Low risk
Herrera-Enriquez and Narvaez-Guerra et al.,[34]	Perú	3635	237	N		53.59	NM	America	NCEP-ATP III	28.69	24.05	22.78	12.66	22.36	26.58	Low risk
Herrera-Enriquez and Narvaez-Guerra et al.,[34]	Perú	3635	237	N		53.59	NM	America	IDF	37.97	37.97	26.58	15.19	20.67	33.75	Low risk
Huang et al.,[12]	China	2060–3820	5053	N	41.8 (13.6)	56.04	100	Asia	CDS	3.6	31.6	8.95	4.8	29.7		Low risk
Hurtado – Arestegui et al.,[48]	Bolivia y Perú	3640–4500	168	R	50.58 (5.79)	52.38	100	America	HMS	27.38						Low risk
Juna et al.,[57]	Ecuador	> 2000	2252	R		65.29	NM	America	NCEP-ATP III	11.23						Low risk
Kapil et al.,[55]	India	2084	979	N		64.04	NM	Asia	IND-DF	28.60	28.60	12.15	18.18	23.19	24.0	Low risk
Lin et al.,[54]	India	3505	149	R	54.7 (16.7)	68.46	NM	Asia	AHA/NHLBI	26.17	13.42	64.43		45.07		Low risk
Lopez-Pascual et al.,[38]	Ecuador	2758–2787	108	R	20.26 (2.63)	45.40	NM	America	IDF-AHA/NHLBI	4.63	81.48	10	4.63	6.48		Low risk
Matsubayashi et al.,[41]	China	3000–3300	393	N	66.7 (5.1)	52.93	0	Asia	ECC-MS	8.40	66.18		10.47	51.40		Low risk
Medina-Lezama et al.,[37]	Perú	2335	1878	R	34.24 (8.08)	53.83	0	America	AHA/NHLBI	18.80	81.48					Low risk
Mejía et al.,[32]	Peru	4100	1198	R	34 (20-67)	7.42	NM	America	IDF	33.30						Low risk
Miele et al.,[35]	Peru	3825	954	R	55.3 (12.3)	51.63	NM	America	AHA/NHLBI. ATP III. IDF. WHO. HC. ECS. JOS	50.04	62.20	18.70	7.40	22.50	62.2	Low risk
Ninatanta-Ortiz et al.,[117]	Peru	−2750	1427	R	12.74 (0.94)	69.52	100	America	NCEP- ATP III	10.51	23.05	39.80	0.84	2.24	0.55	Low risk
Orces and Gavilanez[46]	Ecuador	> 2000	2298	R	71.6 (8.1)	54.69	29.9	America	JIS	57.43						Low risk
Porchia et al.,[49]	Mexico	2135	433	R		56.35	NM	America	HMS	62.12						Low risk
Reyes Jiménez et al.[52]	Mexico	2240	770	R	18 - 65	60.00	NM	America	NCEP-ATP III	52.59						Low risk
Salazar-Lugo et al.[45]	Ecuador	2200	233	R	47.40 (12.99)	53.20	100	America	IDF	34.33	63.29					Low risk
Sanchez-Samaniego et al.[39]	Peru	1900–3900	385	N		61.04	NM	America	JIS	21.3						Low risk
Sherpa et al.[58]	China	3700	692	N		54.19	0	Asia	IDF	8.24	41.90	7.66	57.51	36.98	3.90	Low risk
Thakur et al.[56]	India	1970	81	N	38.2 (9.9)	37.29	56	Asia	IDF	63.56	95	100		100		Low risk
Thakur et al.[56]	India	1970	81	N	38.2 (9.9)	37.29	56	Asia	NCEP-ATP III	68.64	64.41			100		Low risk
Continued																

Author	Country	Altitude level	Sample size	Type of inhabitant	General characteristics			Continent	Definition of MetS	Prevalence of MetS (%)						Quality score (Max. 9)
					Age (mean ± SD years or median (IQR))	Female (%)	Urban (%)			Total	Abdominal perimeter (%)	High level of trigliceridos (%)	Alteration of blood glucose (%)	Blood pressure (%)	Low HDL (%)	
Peng et al.[42]	China	> 4000	920	N		54.46	NM	Asia	NCEP-ATP III	32.83	62.06	11.85	8.26	36.74	83.69	Low risk
Peng et al.[43]	China	2800	920	R	43.2 (13.9)	54.46	NM	Asia	NCEP-ATP III	31.19	55.76				86.3	Low risk

Table 1. Baseline characteristics of studies assessing the prevalence of metabolic syndrome at altitude worldwide (n=28). NR: Not reported, R: Residente, N: Native, NM: not mentioned, HDL: high density lipoproteins, IDF: International Diabetes Federation, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III, ECC-MS: Examination Committee of Criteria for Metabolic Syndrome (Japan), AHA/NHLBI : American Heart Association/National Heart, Lung and Blood Institute, JIS: Joint Interim Statement, CDS: Chinese Diabetes Society, HMS: Harmonizing the metabolic síndrome, LAC-HTA-D_MS: Latin American Consensus on the management of hypertension in the patient with diabetes and the metabolic síndrome, IND-DF: Indian Diabetic Federation, WHO: World Health Organization, HC: Health Canada, ECS: European Cardiovascular Societies, JOS: Japanese Obesity Society, CTF: Cooperative Task Force.

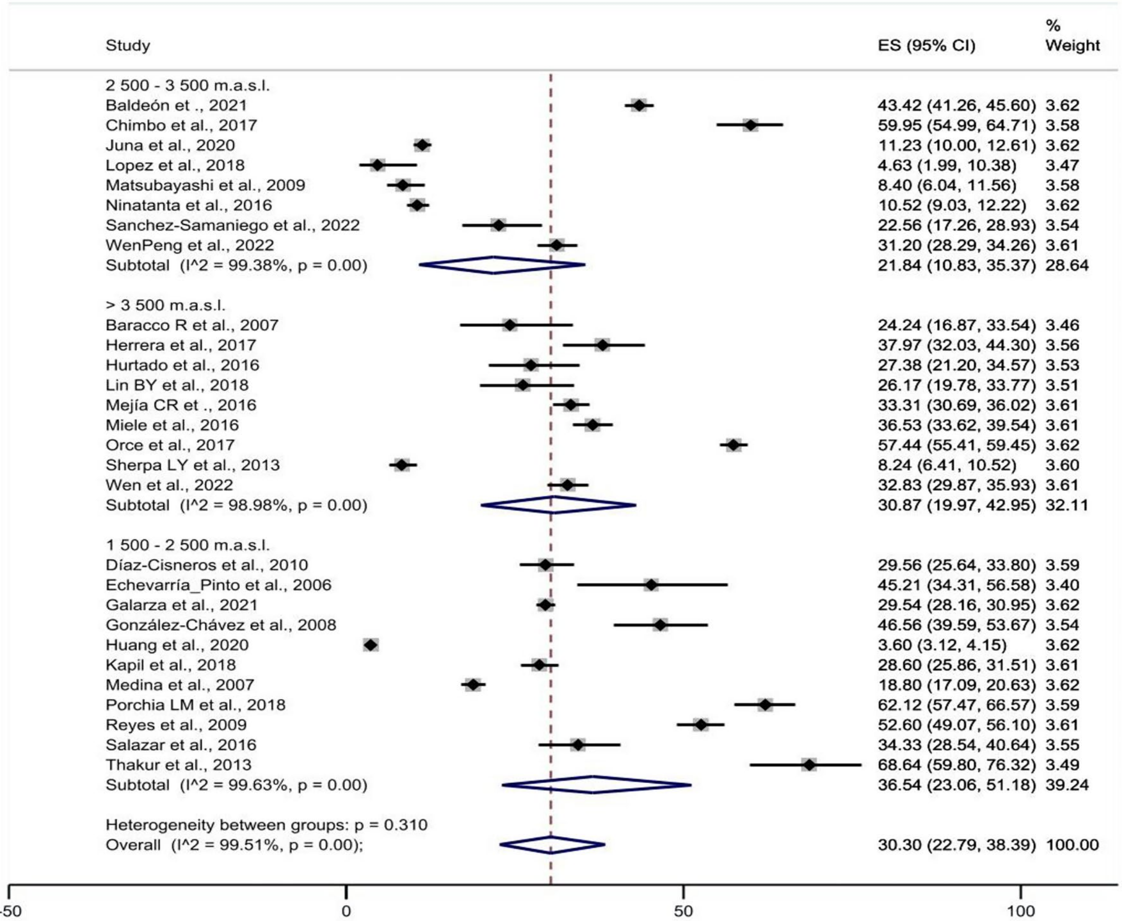

Fig. 2. Forest plot of the prevalence of metabolic syndrome by altitude levels

Prevalence of metabolic syndrome overall and by subgroups (%)										
			Age group		Type of resident			Level of altitude		
Overall prevalence of the metabolic syndrome	Sex prevalence		< 55 yr (%)	>= 55 yr (%)	Rural (%)	Urban (%)	Mixt (%)	1500–2500 m.a.s.l. (%)	2500–3500 m.a.s.l. (%)	> 3500 m.a.s.l. (%)
	Global		28.30	42.40	26.40	25.00	32.90	36.50	21.80	30.90
	Male	26.80%	23.60	41.30	16.20	25.50	30.50	34.40	21.70	18.70
	Female	35.50%	29.10	63.70	28.20	37.50	37.10	38.70	33.40	31.70

			Continent			Type of definition		Type of population	
30.30%	Sex prevalence		America (%)	Asia (%)	IDF (%)	NCEP-ATP III (%)	Another (%)	Resident (%)	Native (%)
	Global		33.20	23.40	29.80	37.30	26.80	33.00	25.60
	Male	26.80%	30.40	18.40	17.90	31.70	29.00	31.40	19.60
	Female	35.50%	33.40	37.70	31.30	40.60	30.60	37.80	31.10

Table 2. Prevalence of metabolic syndrome overall by subgroups (n=28). NR: not reported, HDL: high density lipoproteins, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III, IDF: International Diabetes Federation, m.a.s.l: meters above sea level.

Blood pressure had a pooled prevalence of 28.4% (95% CI 17.2–41.1%; I^2: 99.6%). Abdominal perimeter with a prevalence of 43.5 (95% CI 34.0–53.2%; I^2: 99.3%). Alteration of blood glucose with a prevalence of 13.2% (95% CI 6.7–21.4%; I^2: 99.4%). The high level of triglycerides had a prevalence of 22.3 % (95% CI 16.0–29.3%; I^2: 97.6%), and the low HDL levels had a prevalence of 43.0% (95% CI 23.1–64.1%; I^2: 99.8%). Which had different results according to the sex Table 2.

Prevalence of metabolic syndrome by subgroups and sex (%)									
Overall prevalence for each component of the metabolic syndrome	Sex	Age group		Type of resident			Level of altitude		
		< 55 yr (%)	>= 55 yr (%)	Rural (%)	Urban (%)	Mixt (%)	1500–2500 m.a.s.l. (%)	2500–3500 m.a.s.l. (%)	> 3500 m.a.s.l. (%)
Abdominal perimeter = 43.5%	Male	8.90	12.20	19.90	24.50	NR	22.10	20.40	25.30
	Female	49.30	35.40	53.60	53.50	44.10	32.70	47.50	70.00
Blood pressure = 28.4	Male	21.50	16.00	24.20	0.90	25.00	24.80	6.10	29.60
	Female	16.70	27.30	27.90	4.70	16.10	24.90	5.30	20.80
High level of trigliceridos = 22.3	Male	33.80	8.00	20.90	39.30	34.00	37.20	24.20	38.70
	Female	21.60	14.50	21.00	38.40	16.50	26.60	17.20	22.40
Low HDL = 43.0	Male	39.00	5.10	29.80	72.40	63.10	25.10	52.60	25.50
	Female	51.50	34.60	9.20	40.70	61.20	46.30	59.40	43.00
Alteration of blood glucose = 13.2	Male	21.50	16.00	28.20	0.90	3.40	7.60	2.20	19.70
	Female	8.30	21.50	28.90	0.50	3.70	8.50	3.10	18.50

Table 3. Prevalence of metabolic syndrome according to age group, type of resident and level of altitude (n=28). NR: not reported, HDL: high density lipoproteins, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III, IDF: International Diabetes Federation, m.a.s.l: meters above sea level.

Prevalence of metabolic syndrome by subgroups and sex (%)								
Overall prevalence for each component of the metabolic syndrome	Sex	Continent		Type of definition		Type of population		
		America (%)	Asia (%)	IDF (%)	NCEP-ATP III (%)	Another (%)	Resident (%)	Native (%)
Abdominal perimeter = 43.5%	Male	13.90	32.50	27.60	15.40	34.90	24.50	19.90
	Female	43.80	51.70	54.20	51.10	28.00	49.00	46.30
Blood pressure = 28.4%	Male	12.90	31.70	29.30	8.30	31.10	16.50	26.90
	Female	8.30	32.00	22.40	6.30	26.40	11.60	27.90
High level of trigliceridos = 22.3%	Male	43.70	11.30	36.40	31.10	7.90	35.00	20.90
	Female	29.50	9.10	17.80	28.10	14.50	20.50	21.00
Low HDL = 43.0%	Male	38.90	25.80	36.30	40.90	5.10	55.80	2.80
	Female	54.60	38.00	48.50	53.30	34.60	61.60	26.10
Alteration of blood glucose = 13.2%	Male	3.10	22.20	14.20	4.00	7.30	2.10	21.60
	Female	3.50	23.70	15.50	3.70	5.40	3.00	20.30

Table 4. Prevalence of metabolic syndrome according to continent, type of definition and type of population (n=28). NR: not reported, HDL: high density lipoproteins, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III, IDF: International Diabetes Federation, m.a.s.l: meters above sea level.

Prevalence of metabolic syndrome according the subgroup analysis and sex

Regarding subgroup analysis by definition, the pooled prevalences were 29.8% (95% CI 18.9–40.7%; I^2: 99.4%) for the IDF group, 37.3% (95% CI 26.9–47.7%; I^2: 99.2%) for ATP III and 26.8% (95% CI 11.5–42.1%; I^2: 99.7%) for the other definitions. In the subgroup analysis by altitude, groups and their pooled prevalences were 1500–2500 m.a.s.l (36.5%; 95% CI 23.1–51.2%; I^2: 99.6%), 2500–3500 m.a.s.l (21.8%; 95% CI 10.8–35.4%; I^2: 99.3%), and > 3500 m.a.s.l (30.9%; 95% CI 20.0–43.0%; I^2: 98.9%). Regarding subgroup analysis by continent, prevalences were 33.2% (95% CI 25.6–41.3%; I^2: 99.2%) for America and 23.4% (95% CI 11.0–38.6%; I^2: 99.5%) for Asian people Tables 3 and 4.

According to type of population, prevalence was 33.0% (95% CI 25.0–41.6%; I^2: 99.3%) for residents and 25.6% (95% CI 12.5–41.5%; I^2: 99.6%) for native people. In relation to type of resident, prevalence was 26.4% (95% CI 14.9–40.0%; I^2: 97.9%) for rural, 25.0% (95% CI 7.2–48.8%; I^2: 99.1%) for urban and 32.9% (95% CI 22.9–43.7%; I^2: 99.6%) for both. Finally, people who is < 55 years had the prevalence of 28.3% (95% CI 21.5–35.2%; I^2: 99.5%) and >= 55 year was 42.4% (95% CI 26.3–58.4%; I^2: 99.4%). The prevalences by sex it can be found in Tables 3 and 4.

Meta-regression analyses

In the meta-regression analyses, no association was found between the type of resident (p=0.188), type of population (p=0.187), continent (p=0.260), level of altitude (p=0.941), type of MetS definition (p=0.214) and male/female sex (p=0.804/0.839) with the prevalence of MetS. Unlike the age group (p=0.002) that did show an association. The residual heterogeneity in the meta-regression was 93.5%.

Quality assessment

More than 80% of the studies met criteria for adequate sample size, detailed description of subjects and setting, appropriate sampling frame and methods, and reliable measurement of conditions in all participants. 76% of the studies met criteria for appropriate statistical analysis. Additionally, most of the studies met criteria for data analysis with sufficient coverage of the identified sample, which could potentially lead to underestimation or overestimation of the prevalence, depending on factors such as the sex and level of altitude of the participants Supplementary Material 4.

Discussion

According our knowledge this systematic review is the first that assesses the prevalence of MetS in altitude regions above 1500 m.a.s.l. worldwide. We found that the prevalence of MetS was 30.3% (> 3500 m.a.s.l: 30.9% vs. < 2500 m.a.s.l: 36.5%) which is inferior to other systematic reviews, which were done at sea level[60–62], as those carried out in Latin American countries with a prevalence of up to 41.0%[53,63], middle eastern countries since 2.2 to 50%[64], India 30.0%[65], Africa 32.4%[66] and people with mental health disorders till 38.7%[67,68]. These differences according to altitude could be attributed to altitude populations having lower risk factors, lower socioeconomic status, higher mineral intake, lower calorie diets, lower rates of obesity and diabetes[10,69]. Likewise, the high-altitude environment influences reduced energy intake and increased resting metabolic rate. Coupled with increased physical activity, driven by agricultural and livestock tasks[15,70,71], all of which decrease the risk factors that lead to a lower prevalence of MetS.

Abdominal obesity, was present in 4 out of 10 of the participants, we observed that women with MetS have a higher prevalence than men. Similarly, an Asian studied identified that in 5 out of 10 participants showed abdominal or centra obesity[72]. Different to a systematic review in Latin America where countries of different altitudes were included and reported in 6 out of 10 residents[61]. It is also lower than another review at sea level (5 out of 10)[73]. Studies on the components of MetS have reported a high prevalence of abdominal obesity in the Latin American population, similar to or even higher than in developed countries, which can be explained by lifestyle changes[61,74]. These reports are not entirely comparable with another study in Latin America showing a high prevalence of abdominal obesity but a low prevalence of hypertriglyceridemia, hypertension, and low HDL values[33]. Overweight, obesity, and related noncommunicable diseases have become major public health problems in the regions, although rates still vary in some countries[75].

In relation to Blood pressure, it was present in 3 out of 10 participants, in which the male sex presents a higher value than the female. Similarly, a reviews carried out in Tibetan settler, where found a prevalence between 2 to 5 out of 10 residents[76,77]. Likewise, it is similar to another study conducted al Altitude in Latin America countries with a prevalence of 1 out of 10[78]. The result is lower than others studies that were carried out at sea level with prevalences reported between 3[79] to 5 residents at sea level[80]. At altitude has been found that living at high altitude is a unique risk factor for hypertension, with a 2.0 % increase in the prevalence of hypertension per 100 m of altitude, which could be due in part to physiological adaptation to hypobaric hypoxia[76].

Regarding Hypertriglyceridemia, it was present in almost 2 out of 10 participants with the male sex being the most affected. Different to reported by studies carried out to sea level, where it found a prevalence between of 4 to 5 out of 10 residents[81,82]. When observing the metabolic components potentially associated with MetS found in the review, it was determined that adiposity, low HDL values, hyperglycemia, and hypertension were mostly reported in the Asian altitude population, a behavior corroborated by another study where hypertension and obesity are strongly associated with a high prevalence of MetS[12,83].

Finally, Hyperglycemia was present in 1 out of 10 participants, result that it was the same for both sexes. This result is similar to that found in systematic reviews carried out at sea level (16.0%)[73]. However, a study carried out in Nepal showed a prevalence of hyperglycemia and MetS was in 3 out of 10 residents[84]. It is relevant to know that hyperglycemia is not the first sign of MetS and develops as a later complication[85]. On the other hand, hyperglycemia is the most prevalent component in Latin America, with 25.0%, which is supported by the fact that hyperglycemia is the least prevalent component, as its prevalence is significantly lower in Asian countries compared to other studies[61,86]. This is supported by the Latin American multicenter CARMELA study, which showed hypertriglyceridemia to be the most prevalent component (85.9%) and glucose the least prevalent (31.2%)[36,87].

Subgroups analyses

Our study found that the prevalence of MetS in rural areas is higher than in urban areas. Our study differs from other systematic reviews and meta-analyses conducted in Brazil and Iran where the prevalence of MetS was higher in urban areas compared to rural areas, 34% vs 15% in Brazil[63] and 0.39% vs 0.26% in Iran[88]. It is also different from what was found in a study carried out in Ghana, where it was evident that the prevalence was higher in urban areas than in rural areas and it could also be evidenced according to sex, in men it was 23.6% in urban areas[89]. While the difference in prevalences is not significant, it probably reflects the multifactorial origin of MetS among populations with their own epidemiological characteristics. However, there is a lack of studies conducted at altitude that show both groups separately.

The finding of the study is that there is a higher prevalence of MetS in the resident population compared to the native population. No similar studies comparing these characteristics were found. This difference could be due to the fact that it has been evidenced that in the native population, due to their own exposure to the hypoxic hypobaric environment, it has been noted that these people present a greater increase of the anorexigenic hormone leptin, which is related to weight loss, especially of the abdominal adipose tissue, which is associated with a lower prevalence of developing MetS[90]. In contrast, the resident population, as observed in the context of Ladakh, often represents a migrant population moving from a high-altitude rural region to a high-altitude city. These residents tend to adopt the lifestyle of rapidly developing countries, which may lead to an increase in the prevalence of all components of the metabolic syndrome compared to those who continue to live at higher altitudes. This phenomenon reflects the different lifestyles and customs that residents bring with them, which may condition the development of a higher prevalence of MetS[54]. Our review did not include studies of populations living at altitudes above 4000 m.a.s.l. due to the scarcity of existing information, which represents a significant limitation. This lack of information leaves a gap in knowledge about the metabolic health of high-altitude inhabitants and underscores the need for more research in these extreme areas. Future studies addressing this gap are needed to better understand how altitude affects the development of metabolic syndrome.

In our study, we found that there is a higher prevalence in individuals aged 55 years or older than younger. Our study differs from another systematic review, where an equal prevalence (42%) was found[63]. Likewise, it is similar to a study carried out in Latin America, where a higher prevalence was reported in subjects over 50 years of age[61]. Additionally, a study carried out in Chile found that as age increases there is an increase in the prevalence of each of the MetS components[91], which is consistent with what was found in our study. Therefore, a person, as they age, is more predisposed to having MetS because they are influenced by the high prevalence of metabolic risk factors developed at these ages[92,93].

We found that American was the continent with the highest reported prevalence de MetS, which can be explained by studies reporting that lifestyle (low fruit and vegetable intake, higher meat consumption, and insufficient physical activity) in that continent are highly adaptive risk factors for this MetS[94,95], in combination with certain genetic factors and metabolic adaptations during fetal life, may be considered causal factors for this disease[74]. Likewise, for example, in Ecuador, a Latin America country, more than 30.0% of the adult population aged 18–59 years has MetS and about 85.0% of the population has at least one metabolic abnormality defined as a disorder of MetS[16], but reports suggest that the prevalence is higher in coastal cities than in high-altitude cities; furthermore due to intake of sugar and excessively processed foods, high consumption of carbohydrates and salt, and sedentary lifestyle[96]. Finally, Asian reported prevalence of MetS (2 out of 10), despite being the largest developing continent in the world and studies reporting a high prevalence of MetS[97] was the lowest reported in high-altitude populations; concerning three different countries, these prevalences may vary due to the diversity of populations, cultural behaviors, and lifestyle[60,98].

It is believed that more than 500 million people worldwide live at altitudes above 1500 m.a.s.l, which causes severe physiological problems for people living in these areas[12]. In our review, the lowest altitude considered, 1500–2500 m.a.s.l, 4 out of 10 inhabitants has a high prevalence of MetS, while the highest altitude, above 3500 m.a.s.l, the prevalence it was present in 3 out of 10. While is that true, genetic and physiological adaptations to altitude determined by hypoxia affect glucose metabolism, leading to appetite suppression and reduced caloric intake[99]. The adaptations may explain why prevalence is lower at higher altitudes. Therefore, future research should focus on proposing reference values for each of the five components that determine MetS in populations at high altitudes because of phenotypic and genotypic differences[100]. The data and studies on MetS components, reference values and cut-off points in different highland regions of the world, particularly in South American countries, are still incipient, and future research should aim to develop new approaches for more accurate assessment, diagnosis, and monitoring of highland populations. However, evidence is lacking as to why at 2500–3500 m.a.s.l. most prevalences are lower, with the exception of low HDL.

The prevalences were 2, 4 and 3 out 10 for IDF, ATP III and other definitions. Unlike, to other systematic review and meta-analysis, the prevalences were 31% (IDF), 31% (ATP III), and 25% (JIS)[63]. And another study that reported prevalences of 54.0% (IDF), 48.0% (AHA/NHLBI), 36.0% (ATP III) and 31.0% (WHO)[53]. We emphasize that the studies mentioned above which have been chosen for comparison correspond to studies carried out with resident populations at sea level and they are systematic reviews. Thus, to the best of our knowledge, our results (at altitude) are lower than at sea level. However, it must be recognized that high altitude regions exhibit certain deficiencies, including primary health care services, unequal access to essential medicines and a significant lack of effective programs for the prevention, treatment and management of chronic diseases[101,102].

In our study, 4 women and 3 men out of 10 had MetS. Similar to other studies, like the Gulf Cooperation Council countries, where a higher prevalence of MetS is reported in women than in men[103]. While it is true, the MetS components probably overlap at the physiological level, and evidence shows that males develop this syndrome earlier than females, as reported in studies of Australian adults and high-altitude populations in China[12,104–106]. The higher prevalence of MetS in women reported in the articles reviewed may also be due to the higher prevalence of adiposity in women (46.0%) than in men (24.0%), according to a report on the current outlook for obesity and hypertension in LATAM, it is projected that by 2025, 80–90% of the population will suffer from hypertension and obesity and consequently acquire MetS, and it has been shown that only people with one or two criteria will show greater development of MetS[105,107]. Globally, statistical trends of physical inactivity reported a higher prevalence in women, explaining women's greater susceptibility to MetS predisposition, this finding is also complemented by a LATAM study on sedentary lifestyles that focused on gender differences reporting that women were less physically active than men[108,109]. The intake of energy-dense foods is associated not only with obesity, but also with impaired glucose regulation, hypertension, and dyslipidemia, leading to an increased risk of MetS[110,111], in our review, we found no significant differences between men and women in hyperglycemia, but there were significant differences in other indicators such as hypertension and hypertriglyceridemia, which were higher in men than in women.

According to several studies, altitude may affect the incidence of MetS from multiple aspects, for example, there is a lower prevalence of obesity and diabetes at higher altitudes[12] also, the prevalence of hypertension in high-altitude residents is lower than in low-altitude residents[13,78].

People residing at high altitudes have physiological adaptations to environmental pressure and reduced oxygen availability, such as elevated hemoglobin concentration, enlarged lung volume and decreased hypoxic ventilatory response[1]. These adaptations have resulted in changes in cardiovascular and respiratory efficiency, lower LDL cholesterol values, higher HDL cholesterol, better-fasting glucose levels compared to sea level residents, and improved blood glucose levels[1] and direct catabolic effect; for example, in BMI there was a reduction of -1.31 kg/m^2 per kilometer of altitude[54].

Some health conditions have also been observed in people living at altitudes, such as acute mountain sickness, pulmonary and cerebral edema at altitude, hypoxia, lack of appetite, fatigue, stomach discomfort, and unwillingness to work. These conditions explain the metabolic risk factors and generate physical restriction and mental depression, consequently promoting the development of cardiometabolic disorders[13]. Regarding lack of appetite, at higher altitudes there is an increase in basal metabolic rate and an increase in leptin levels, leading to lower calorie intake due to lack of appetite[112]. Also, hypoxia leads to appetite suppression by impairing glucose metabolism[90] and, consequently, there is a reduction in caloric intake[1] and a lower prevalence of obesity[90]. Evidence to support our results in each of the components of the MetS.

Implications of the results and recommendations for future studies

There are few systematic reviews related to altitude[22]. In several regions of the world, the prevalence of MetS tends to increase, and it occurs more frequently in women; it is also mentioned that it is considered a public health problem and needs to be controlled to mitigate this pathology. MetS is a disease in constant increase worldwide. Populations located at altitude present differences with respect to those located at sea level, such as their lifestyles, customs and hypoxic hypobaric environment. MetS causes high public health expenditure, however, being a pathology with modifiable risk factors, the impact on the economy is substantial[113]. These risk factors should be reduced through prevention focused on rural and high-altitude areas, where costs, access to health services and knowledge of the disease are lower[101]. Thus, it is suggested that the prevalence and characteristics of the most frequent components of MetS vary among different ethnic groups and may not be specific to each group or race.

The prevalence of MetS is increasing in parallel with the rising prevalence of obesity and is projected to increase by 33.0% over the next two decades and by 2030 (51.0%) of the population will be obese. If these predictions prove accurate, efforts to reduce healthcare costs will be further hampered, and the incidence of cardiovascular disease could spiral out of control as a consequence[114]. Curiously, in developed countries, there is a transition in which the higher socioeconomic class reduces metabolic risk while it increases in the lower social classes[115,116]. This possibly indicates that the assumption of a healthier lifestyle occurs in the wealthier classes than in those who are not and are exposed to a health system that is not 100% covered. Therefore, prevention strategies are needed that identify sociodemographic and environmental factors (which especially affect women) and target risk behaviors that can be modified, such as being underweight, prolonged sedentary behavior, and diet. Our result diverges from that reported in studies performed at sea level, so we assume that there is an inverse relationship between altitude and the prevalence of MetS.

We recommend that further studies assess the prevalence of the components and examine the impact of educational measures and lifestyle modification on the prevalence of MetS Similarly, further studies should be developed to compare the prevalence of MetS between populations living at high altitude and those living at sea level and to identify associated risk factors for reversal. Therefore, epidemiological estimates of MetS risk factors and their frequency are essential to develop specific management programs and plan an optimal allocation of healthcare resources for this patient population.

Limitations and strengths

The study has some strengths. First, this is the first systematic review and meta-analysis on the prevalence of MetS in high-altitude populations worldwide so that it may serve as a baseline for future studies, and the systematized information may be helpful, not only for researchers but also for public health professionals working in high-altitude regions and even for the development of national strategies for the prevention and treatment of MetS in mid- and high-altitude regions. Second, we reviewed peer-reviewed publications without language restriction to gain a comprehensive and culturally informed understanding of the topic. Third, we addressed a clear gap in the literature in considering altitude residents for characteristics unique to the characteristics associated with the hypoxic hypobaric environment. This study also has limitations. The prevalence estimates of MetS were not standardized due to the study sample selection and statistical methods of the included studies. Second, there was a considerable heterogeneity due to unmeasurable variables such as nutritional patterns in each country, physical activity, and healthy lifestyles in each population. These limited their comparability. Nevertheless, we have used the best available data to increase our understanding of this important topic. An additional limitation is that we did not include well-designed peer-reviewed studies that took into account socioeconomic factors, cultural factors, ethnics factors, hypoxemia, and the effects of altitude above 3500 m.a.s.l. on the components of the MetS because there is limited information available, otherwise it would have provided a more complex and culturally informed understanding of the subject, especially in relation to inhabitants residing in regions with higher altitude. Despite our thorough review with no language restrictions, the lack of studies considering socioeconomic, cultural, and hypoxemic factors, along with variability in MetS definitions, may have impacted the accuracy and generalizability of the results. Additionally, studies focused on migrant or urban populations may not fully capture the effects of altitude on native residents. Therefore, we recommend that future research include well-designed studies at altitudes above 4000 m.a.s.l. and consider socioeconomic and cultural effects, as well as differences in definitions of MetS. It is also crucial to explore the interaction between age, altitude, and prevalence of hypertension, as well as variations in waist circumference among different ethnic groups.

Conclusion

The prevalence of MetS at altitude (> 1500 m.a.s.l.) was 36.5%, being higher in women (35.5%). It was observed that there is an inverse relationship between higher altitude and the prevalence of MetS. Among its components, abdominal obesity and low HDL were present in more than 40.0%, while high blood pressure, high triglycerides and impaired glucose were present in less than 30.0%. We recommend that our results be considered for future research in populations living at altitude since they have different characteristics from populations at sea level.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Received: 24 February 2024; Accepted: 28 October 2024
Published online: 11 November 2024

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J.P Z-V and P G-E were responsible for the conceptualization, methodology, investigation, data curation, writing—original draft preparation, and writing—review and editing. MR C-M, A-D CS, EA. H-B, J T-F, A P F, J P-M and VA B-Z were responsible for the methodology, investigation, writing—original draft preparation, and writing—review and editing. All authors have read and agreed to the published version of the manuscript

Funding

The study was self-financed.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-77928-z.

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