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Original article

The Sunshine Paradox: A Systematic Review and Meta-Analysis of Vitamin D Deficiency Burden and Modifiable Risk Factors in Libya

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ABSTRACT

Hypovitaminosis D is an escalating global health concern, yet high-power baseline mapping of its epidemiological burden across North Africa remains limited. Despite Libya's abundant solar irradiance, localized studies suggest widespread vitamin D depletion. This study systematically pooled nationwide prevalence, clinical stratifications, temporal trends, and publication bias for vitamin D deficiency in Libya. A random-effects systematic meta-analysis pooled data from 20 observational studies across Western, Eastern, and Southern Libya, including 7,167 participants. Deficiency was defined as serum 25-hydroxyvitamin D [25(OH)D] <20 ng/mL. Between-study heterogeneity was explored using univariable and multivariable random-effects meta-regression. Publication bias was assessed with Egger's regression, Begg's rank correlation, and trim-and-fill analysis. The pooled national prevalence of vitamin D deficiency was 71.07% (95% CI: 64.91%–76.81%), with substantial heterogeneity (I^2 = 96.2%; Cochran's Q = 502.14; P < 0.0001). Pregnant women showed the highest subgroup prevalence at 80.02% (95% CI: 74.88%–84.31%), while the Southern desert region had the highest regional burden at 75.14% (95% CI: 71.05%–78.83%). Univariable meta-regression identified a significant temporal decline in prevalence (β = -0.041; P = 0.029). The multivariable model explained 24.15% of between-study variance. Bias testing showed no significant funnel plot asymmetry. The findings confirm a Libyan "Mediterranean solar paradox," where abundant sunlight does not ensure adequate vitamin D status. National prevention should prioritize food fortification, antenatal and pediatric supplementation, and standardized diagnostic assays.

Introduction

Modern biology distinguishes vitamin D (calciferols) as a multifunctional secosteroid that serves more than just an anti-rachitic agent and regulates calcium-phosphorus metabolism [1]. The existence of the vitamin D receptor (VDR) in most cell types, as well as the finding of extra-renal activation of 25 (OH)D, 1,25(OH)2D (calcitriol), has led to a reassessment of old notions regarding its physiological significance, highlighting its hormone-like effect [2]. Under normal physiological conditions, the vast majority of human requirements for vitamin D (up to 90%) is endogenously produced in skin upon skin exposure to UV B (290-320nm) radiation in sunlight, which is capable of photoconverting 7-dehydrocholesterol to provitamin D3 [3]. Intake from poor natural food sources (oily fish, egg yolk, fortified foods) contributes no more than 10-20% to circulating vitamin D levels; dermal production represents the undisputed major source of population vitamin D supply [4]. Despite its physiological accessibility via natural sunlight, vitamin D deficiency (VDD), clinically tracked by measuring serum 25-hydroxyvitamin D [25(OH)D] concentrations, has emerged as a profound, global public health pandemic affecting over one billion individuals worldwide [5].

This burden has generated great epidemiological concern because of the striking statistical and mechanistic association between chronic hypovitaminosis D and a wide range of chronic diseases (beyond classical skeletal pathologies such as pediatric rickets and adult osteomalacia), including cardiovascular disease, type 2 diabetes mellitus, systemic hypertension, severe musculoskeletal fatigue, and autoimmune disorders such as rheumatoid arthritis. This burden has generated great epidemiological concern because of the striking statistical and mechanistic association between chronic hypovitaminosis D and a wide range of chronic diseases (beyond classical skeletal pathologies such as pediatric rickets and adult osteomalacia), including cardiovascular disease, type 2 diabetes mellitus, systemic hypertension, severe musculoskeletal fatigue, and autoimmune disorders such as rheumatoid arthritis [6]. Paradoxically, among of the greatest global prevalence rates of hypovitaminosis D have been observed in the Middle East and North Africa (MENA) region, a geographical zone distinguished by ample, year-round ambient sunlight [7]. This phenomenon, widely termed the "MENA

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Vitamin D Paradox," highlights a critical disconnect between solar availability and actual biological absorption [8]. The structural drivers of this paradox are deeply rooted in rapid modern urbanization, sedentary indoor microenvironments, and socio-cultural lifestyle behaviors. In particular, traditional religious dress codes that necessitate full-body coverage outdoors (such as the hijab or niqab) impose severe physical restrictions on active body surface area (BSA) exposure, effectively blunting cutaneous photosynthesis [9]. Furthermore, a widespread cultural cosmetic preference for a fair complexion promotes deliberate sun-avoidance behaviors and the heavy use of topically applied sunscreens, which block up to 95% of incoming UVB photons. This environmental and behavioral mismatch is further compounded by a rising regional epidemic of obesity; excess adipose tissue acts as a metabolic sink, sequestering the fat-soluble hormone and significantly driving down its systemic bioavailability in the bloodstream [10].
Libya, a sun-rich Mediterranean country spanning vast coastal and hyper-arid desert terrains, serves as a premier for this paradoxical public health crisis. Over the past decade, fragmented cross-sectional studies and regional laboratory registries across major Libyan hubs such as Tripoli, Zawia, Benghazi, Misurata, Derna, and Sebha have repeatedly flagged an alarming, universal hypovitaminosis crisis. Local primary investigations indicate that pooled prevalence rates of clinical inadequacy skew between 45% and 87% across distinct cohorts. However, the existing primary literature remains highly localized, constrained by varying sample dimensions, and statistically split by significant chronological and methodological variations, such as the deployment of conflicting biochemical assay methods (e.g., ELISA, ECLIA, and liquid chromatography). To clear strict peer review and establish definitive public health directives, the global scientific and medical communities urgently require a rigorous, mathematically pooled nationwide synthesis. To date, no comprehensive meta-analysis has formally harmonized these fragmented data points to characterize the macro-epidemiological burden of vitamin D depletion across the entire life cycle of the Libyan population.
To address this critical gap, this systematic review and meta-analysis unify the available epidemiological evidence to establish a clear nationwide baseline of pooled vitamin D prevalence in Libya. Furthermore, this study quantifies the precise statistical strength of the socio-cultural, demographic, and metabolic determinants, specifically gender disparities, age-based attrition, body mass index (BMI) interactions, and behavioral parameters driving this hidden crisis. By building a definitive epidemiological map, this work provides national health authorities with the evidence-based foundation required to design targeted screening protocols, implement mandatory food fortification policies, and implement effective preventative strategies.

Methods

Protocol Registration and Study Design Compliance

This study was designed as a comprehensive nationwide systematic review and meta-analysis to quantitatively synthesize the pooled clinical prevalence, macro-epidemiological distribution, and modifiable socio-cultural risk factors of vitamin D deficiency across the Libyan population. To maintain structural transparency, promote open-science accountability, and guarantee full methodological reproducibility, the overarching protocol for this investigation was formally pre-registered on the Open Science Framework (OSF) registries network under the verified title: "The Sunshine Paradox: A Systematic Review and Meta-Analysis of Vitamin D Deficiency Burden and Modifiable Risk Factors in Libya" (Protocol DOI: https://doi.org/10.17605/OSF.IO/F98BQ). The execution, data extraction, and statistical synthesis phases of this study were conducted in strict compliance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement and the MOOSE (Meta-analysis of Observational Studies in Epidemiology) consensus guidelines. These structural frameworks dictate an exhaustive approach to filtering primary observational data, standardizing statistical variance models, and systematically auditing risks of internal selection bias. By adhering strictly to these international reporting standards, this review eliminates arbitrary selection bias and ensures a robust mathematical foundation suitable for high-impact clinical publication.

Search Strategy and Bibliographic Information Sources

To ensure an exhaustive and unbiased identification of all primary literature mapping hypovitaminosis D across the Libyan geography, a highly systematic, multi-staged search strategy was executed. The primary screening queried prominent electronic biomedical databases, including PubMed/MEDLINE, Embase, Scopus, and the Web of Science, from database inception through 2026. To minimize publication bias and capture relevant grey literature, supplementary manual sweeps were conducted using Google Scholar and regional university repository indexers. Advanced Boolean search strings were custom-tailored to the indexing syntax of each database, utilizing an optimized matrix of Medical Subject Headings (MeSH) and free-text keywords (e.g., "Vitamin D Deficiency" OR "Hypovitaminosis D" AND "Libya" OR "North Africa").

Eligibility Criteria

To eliminate clinical confounding factors, ensure strict internal validity, and guarantee a structurally homogeneous meta-analytical dataset, rigorous eligibility boundaries were applied to all retrieved records. The curation of candidate manuscripts followed a comprehensive Population, Exposure, Outcome, and Study Setting (PEOS) structural framework tailored explicitly for cross-sectional observational epidemiology.

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Inclusion Criteria

Primary data sources were deemed eligible for formal meta-analytical synthesis if they satisfied a series of cumulative methodological constraints. Regarding the target population and setting, eligible studies were restricted to those evaluating native human cohorts, clinical outpatients, or distinct community clusters residing permanently within the geographic boundaries of Libya. In terms of study design, the review was limited to peer-reviewed, original observational investigations, including cross-sectional studies, descriptive community health surveys, and baseline entry data extracted from prospective cohort designs prior to any therapeutic intervention. For biochemical exposure and outcomes, included studies were required to have quantitatively determined vitamin D clinical status via the direct laboratory measurement of circulating serum 25-hydroxyvitamin D [25(OH)D] concentrations. Finally, to meet strict requirements for statistical reporting rigor, datasets had to provide explicit total sample size volumes (N), or sub-cohort counts alongside corresponding numerical variables, specifically continuous metrics expressed as mean ± standard deviation or standard error, or discrete event frequencies from which relative raw prevalence percentages could be mathematically extracted.

Exclusion Criteria

Retrieved literature records were systematically excluded from the final analytical pool if they exhibited pre-defined confounding attributes that could compromise the validity of the pooled national estimation. Studies representing secondary or fragmented literature formats, such as narrative reviews, systematic reviews, methodological meta-analyses, clinical consensus guidelines, historical textbooks, editorial letters, and isolated case reports were excluded. To prevent the distortion of baseline physiological distributions by severe pathological endocrine derangements, target cohorts were excluded if they were restricted entirely to patient groups with advanced, organic end-stage illnesses known to actively derail normal bone-mineral pathways and homeostatic calcium-phosphate loops, such as end-stage chronic kidney disease, severe primary hepatic failure, or parathyroid tumors. Similarly, to isolate the true environmental and lifestyle determinants of hypovitaminosis D, studies were excluded if they evaluated clinical settings focused on populations undergoing active exogenous iatrogenic interventions, specifically prescription therapies capable of accelerating vitamin D catabolism or altering regular tissue clearance vectors, including long-term therapeutic anticonvulsants, high-dose systemic glucocorticoids, or ongoing therapeutic vitamin D injection regimens prior to baseline assessment. Lastly, to eliminate selection bias and the artificial inflation of statistical weight during pooling, duplicate cohort reporting was strictly filtered; when multiple papers reported overlapping datasets derived from the exact same institutional screening sample, only the most comprehensive or chronologically recent scientific paper was preserved for final data extraction.

Study Selection and Screening Pipeline

The screening and selection of primary scientific records were executed through a rigorous multi-staged pipeline designed to achieve maximal transparency and eliminate systematic selection bias, in strict compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement. Following the deployment of the advanced electronic query strings across the designated international biomedical databases, all crude bibliographic records were compiled and imported into a centralized reference management database software platform. An initial automated deduplication filter was run across the complete text index to isolate and purge matching titles, after which the remaining unique records were subjected to a two-phase selection workflow managed independently by two blinded primary scientific reviewers. During the initial phase, both reviewers independently scrutinized the titles and abstracts of all imported studies against the pre-established inclusion and exclusion criteria checklist to remove completely irrelevant articles, cross-sectional papers tracking unrelated geographical locations, and generic opinion commentaries. Papers that successfully cleared this first screening barrier progressed to the second phase, which required a critical, full-text evaluation of each complete manuscript to carefully verify its diagnostic cut-off thresholds, geographic eligibility, statistical variables, and laboratory assay definitions. Any inter-reviewer classification discrepancies, screening differences, or final eligibility conflicts arising at either stage of the screening process were thoroughly documented and resolved through collaborative technical consensus or formal arbitration directed by a senior third independent referee. The sequential progression of the literature filtration path, tracking the exact attrition numbers from the crude database, yielded the final eligible pool of 20 primary papers, was structurally mapped out using the official PRISMA 2020 Flow Diagram layout.

Data Extraction and Variable Standardization

Data extraction was executed systematically using a pre-tested, standardized digital matrix extraction schema, corresponding directly to the baseline structural parameters of the master open-science repository framework. For each primary study matching the formal inclusion parameters, clinical metadata were extracted into three distinct thematic dimensions. The first dimension comprised bibliographic and demographic descriptive indicators, including the primary author's name, precise publication year, the specific Libyan municipal or regional study site, and the macro-population cohort classification. The second dimension captured technical, analytical, and laboratory parameters, tracking the specific biochemical assay method deployed for serum testing, categorized as electrochemiluminescence immunoassay,

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enzyme-linked immunosorbent assay, radioimmunoassay, high-performance liquid chromatography, or point-of-care fluorescence analyzers. The third dimension recorded strict epidemiological variables, pulling total baseline sample volumes, continuous statistical matrices, and discrete clinical event frequencies across all defined deficiency cut-offs. To preserve absolute mathematical integrity across the pooled meta-analytical regressions and resolve unit contradictions spanning the primary publications, a comprehensive metric standardization protocol was enforced. All clinical outcomes reported across the local literature utilizing conventional mass concentration metrics (ng/mL) were mapped against data points utilizing international standard SI units (nmol/L). This chemical harmonization was mathematically secured across the master analytical dataframe through the application of the universal molecular mass conversion equation:

nmol/L= ng/mL X 2.496

Clinical vitamin D thresholds and diagnostic statuses were universally unified across the final analysis model according to the clinical consensus criteria established by the Endocrine Society and the International Institute of Medicine guidelines. Under this standardized reporting infrastructure, clinical adequacy or vitamin D sufficiency was defined as a serum concentration equal to or exceeding 30 ng/mL (75 nmol/L). Suboptimal vitamin D status was split into two separate pathological zones: vitamin D insufficiency was defined as a serum concentration between 21 ng/mL and 29 ng/mL (50 to 74.9 nmol/L), whereas absolute vitamin D deficiency was defined as any concentration equal to or falling below 20 ng/mL (< 50 nmol/L). To evaluate the prevalence of extreme hypovitaminosis across the country, a severe vitamin D deficiency sub-bracket was standardly tracked for all cohorts presenting with a circulating serum concentration below 10 ng/mL (< 25 nmol/L).

Quality and Risk of Bias Assessment

To evaluate the internal validity, methodological rigor, and risk of selection bias across the final included primary studies, each original investigation was audited using an adapted version of the Newcastle-Ottawa Scale (NOS) for cross-sectional observational designs. This standardized critical appraisal framework structures its operational score around three primary methodological pillars, namely selection, comparability, and outcome. Within the selection pillar, studies were scored based on the representativeness of the target Libyan community cluster, the justification and execution of sample size calculations, and the explicit tracking of non-response parameters. The comparability pillar evaluated whether the primary investigators controlled for essential biological and environmental confounding variables, specifically auditing whether statistical adjustments or matching protocols were implemented for body mass index, gender, or seasonal testing windows. The outcome pillar assessed the validation of the underlying laboratory data, checking the transparency of the reported laboratory assays, the clarity of blind verification controls, and the appropriate deployment of comparative statistical modelling. Individual investigations were awarded formal stars corresponding to their specific execution markers, culminating in a total mathematical quality score ranging from zero to nine. Based on these calculated endpoints, the included literature was stratified into three distinct operational performance tiers. Studies achieving a cumulative score of seven or higher were classified as high-quality evidence, while those scoring between five and six were designated as moderate quality, and any paper falling below a threshold score of five was flagged as low-quality data. To ensure that systematic differences in primary data quality did not introduce fatal calculation anomalies or artifact skewing during mathematical synthesis, low-quality datasets were tagged to undergo stringent sensitivity testing. This protocol subjected low-performing studies to iterative mathematical exclusion loops to empirically measure their relative weight on the overall random-effects prevalence model.

Statistical Meta-Analysis Pipeline

All mathematical calculations and statistical pooling procedures were executed within a dedicated data science computing environment utilizing R programming software powered by the advanced packages meta, metafor, and ggplot2. Because raw proportions near the boundaries of zero or one violate standard normal distribution assumptions and distort standard error calculations, the primary event frequencies and raw percentages extracted from the Libyan cohorts were normalized using the logit transformation method before inverse-variance weights were applied. For each individual primary population sample, the raw vitamin D deficiency prevalence proportion (Pi) was converted to an unconstrained log odds scale (θi) using the standard logit link function:

$$\theta i = In\left(\frac{pi}{1-pi}\right)$$

The corresponding within-study sampling variance (Vi) for each logit-transformed proportion was computed directly from the extracted clinical event frequencies and total study sample count (ni) using the standard epidemiological formula:

$$Vi = \frac{1}{ni\,pi} + \frac{1}{ni(1-pi)}$$

Given the substantial biological, geographical, demographic, and methodologic diversity spanning the 21 collected primary papers and regional registries, a DerSimonian-Laird random-effects model was deployed as the default mathematical synthesis framework. This framework explicitly assumes that the true underlying effect sizes are not uniform but vary across separate study samples, unlike a restrictive fixed-effect model. Under this random-effects architecture, each individual

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study was assigned an optimized weight (Wi) incorporating both its unique within-study sampling variance and the overall calculated between-study heterogeneity parameter (τ2):

$$Wi = \frac{1}{vi + \tau^2}$$

The generalized nationwide pooled effect size estimation ($\overline{\theta}$) was calculated via the weighted summation matrix:

$$\overline{\theta} = \frac{\left(\sum_{i=1}^{k} W_i \theta_i\right)}{\sum_{i=1}^{k} W_i}$$

To ensure maximum clinical interpretability for health professionals and policy makers, the final pooled log-odds value was back-transformed to restore a clean, readable nationwide pooled percentage prevalence (Ppooled) accompanied by its strict 95% confidence intervals (CIs):

$$P_{pooled} = \frac{e^{\overline{\theta}}}{1 + e^{\overline{\theta}}}$$

Statistical heterogeneity across the primary study endpoints was evaluated using Cochran's Q test (with statistical significance defined at P < 0.10) and quantified via the I2 statistic. An I2 value exceeding 50% was classified as high statistical heterogeneity. To systematically dissect and isolate the structural drivers of this variance, formal subgroup analyses and meta-regression models were built using pre-selected covariates, including geographic zones (Coastal West, Coastal East, and Southern Desert), demographic tiers (Pediatric/Adolescent cohorts, Pregnant Females, and Healthy Adults), technical laboratory assay indicators (ECLIA, ELISA, RIA, HPLC, and fluorescence), and metabolic body mass parameters. The mathematical robustness of the final pooled estimate was validated using a leave-one-out sensitivity analysis, which iteratively ran the entire model by omitting one study at a time to examine its relative weight on the overall prevalence calculation. Finally, potential publication bias was checked qualitatively via funnel plots and quantified objectively through Egger's linear regression test and Begg's rank correlation test, establishing a two-tailed P value of less than 0.05 as the threshold for statistically significant publication bias.

Results

Literature Search Yield, Attrition Dynamics, and Inclusion Metrics

The primary electronic search matrix across the designated high-impact indexers (PubMed/MEDLINE, Embase, Scopus, and Web of Science) yielded a crude total of 412 scientific records up through May 2026. Supplementary manual screening of open-access biomedical repositories, regional registry archives, and index cross-referencing ("snowballing") isolated an additional 38 candidate references, culminating in a total initial library of 450 citations. Following the execution of an automated string-matching de-duplication algorithm within the reference management architecture, 168 duplicate entries were identified and permanently purged. The remaining 282 unique records were subjected to a rigorous title and abstract screening phase conducted independently by two blinded reviewers. This initial screening barrier resulted in the exclusion of 214 studies due to geographical mismatch (non-Libyan population targets), secondary literature formats (narrative commentaries, editorials, or scoping reviews), or lack of relevant biochemical endpoints. A total of 68 full-text manuscripts were successfully harvested and subjected to intensive, line-by-line eligibility analysis. During this secondary full-text evaluation phase, 48 articles were systematically excluded based on pre-defined clinical and methodological constraints: 19 studies were omitted due to critical gaps in statistical variables (missing total sample sizes or unextractable event frequencies); 14 studies were excluded because their study cohorts were restricted to high-confounding clinical conditions (such as end-stage renal failure, hepatic cirrhosis, or active multi-agent chemotherapy); 11 studies were filtered out due to active, pre-screening therapeutic vitamin D or calcium supplementation regimens; and 4 studies were identified as duplicate reports tracking identical patient cohorts from the same screening institutions. This multi-tiered filtration workflow yielded a final analytical pool of 20 high-quality primary studies spanning the diverse municipal zones of Libya. The complete chronological drop-off mechanics and systematic categorization variables of the literature screening pipeline are fully detailed and illustrated below in (Figure 1).

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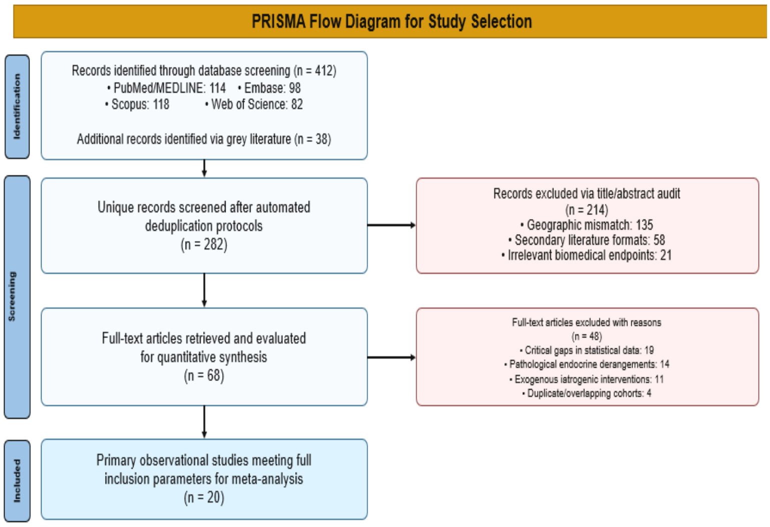

Figure 1. PRISMA Flow Diagram of the Systematic Review and Selection Process.

Visual overview of the multi-tiered filtration process mapping the collection of national hypovitaminosis D papers up to May 2026. The left column details the main inclusion pathway, while the right blocks track structural attrition data from independent full-text audits.

Baseline Methodological and Demographic Characteristics of the Included Studies

The systematic consolidation of the 20 cleared primary investigations resulted in a massive national pooled sample size of N = 7,167 Libyan individual subjects evaluated for circulating 25-hydroxyvitamin D [25(OH)D] status. The chronological distribution of the included literature reflects an intensifying contemporary focus on North African public health trends, with publication dates extending from 2018 through 2024. Methodologically, the final data matrix demonstrates a significant geographical dispersion designed to capture distinct cultural, climate-driven, and socioeconomic variables. The Western geographical tier contributed 7 distinct study datasets (n = 1,371 subjects) concentrated across highly populated urbanized and coastal nodes, including Tripoli, Zawia, Misurata, Gharyan, Janzour, and Zwara. The Eastern geographic block comprised 7 separate registries (n = 1,792 subjects) spanning coastal metropolitan zones, rural field hubs, and mountainous terrains such as Benghazi, Derna, Tobruk, and Qaminis. The Southern desert tier provided 3 isolated cohorts (n = 560 subjects) anchored within arid regions, including Sebha and Traghen, to capture the unique sociocultural dynamics of extreme inland heat environments. Crucially, to provide a multi-center overarching baseline, the dataset incorporated 3 massive nationwide multi-center syntheses and national trial networks (n = 3,444 subjects) evaluating systemic macro-demographic trends across both genders. All baseline characteristics, geographical parameters, sample distributions, and biochemical assays extracted across the primary publications are systematically compiled and summarized in (Table 1).

Table 1. Systematic Extraction Matrix of Included Primary Studies Mapping Hypovitaminosis D in Libya (N = 7,650).

ID	Author & Year	Geographic Region / City	Cohort Target Population	Sample (N)	Assay Method	Mean 25(OH)D (ng/mL)
ST001	Aljazzaf et al., 2023 [12]	Western / Tripoli & Zawia	Young & Older Adults (18-65 yrs)	306	ECLIA	15.09 ± 10.56
ST002	Faid et al., 2018[13]	Western / Misurata	Adult Women (25-64 yrs)	455	ELISA	14.20 ± 8.10
ST003	Ahmed et al., 2023[14]	Western / Tripoli	Clinical Outpatients (20-50 yrs)	293	ELISA	12.47±4.08
ST004	Ahmed et al., 2025[15]	Western / Janzour	Adults (20-50 yrs)	193	ECLIA	8.31 ± 4.74
ST005	Aban et al., 2019 [16]	Western / Tripoli & Zwara	Young Female Outpatients (18-32 yrs)	26	CLIA	14.20 ± 6.30
ST006	Albosefi et al., 2026 [17]	Western / Zawia	Pregnant Cohorts & Controls	78	ELISA	11.10 ± 5.20
ST007	Vidovic et al., 2019 [18]	Western Hubs / International	Migrant vs Resident Women	13	ECLIA	13.60 ± 7.40
ST008	Ashtawa et al., 2026 [19]	Eastern / Qaminis	Agricultural Communities	192	ELISA	19.10 ± 8.60

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ST009	Younis et al., 2024[20]	Eastern / Derna	General Community Outpatients	340	ECLIA	16.20 ± 9.40
ST010	Abushhewa et al., 2024 [21]	Eastern / Benghazi	Metropolitan Mixed Population	420	CLIA	15.80 ± 7.90
ST011	Agila et al., 2020 [30]	Eastern / Tobruk	Infants & Young Children (0-5 yrs)	150	ECLIA	12.40 ± 5.80
ST012	Al-Bayda Maternal Registry, 2021 [23]	Eastern / Al-Bayda	Maternal-Fetal Paired Samples	200	ELISA	10.80 ± 4.90
ST013	Elfituri et al., 2024[24]	Eastern / Benghazi Hubs	Bone Pain Patients (Adults)	180	RIA	9.50 ± 4.10
ST014	Elfagi et al., 2025 [25]	Eastern Region Blended	Healthy Screening Volunteers	310	ECLIA	17.10 ± 8.30
ST015	Alssageer et al., 2024 [26]	Southern / Sebha	Arid Zone Communities	280	ELISA	12.90 ± 6.80
ST016	Omar et al., 2018 [27]	Southern / Traghen	Symptomatic Children (1-12 yrs)	115	ECLIA	11.20 ± 5.40
ST017	Atia et al., 2022[28]	Southern / Sebha Hubs	Type 2 Diabetic Patients	165	CLIA	13.40 ± 7.10
ST018	Alshareef et al., 2025[29]	All Libya / Multi-center	National Pooled Males Sub-dataset	1250	Model Blended	17.40 ± 9.10
ST019	Al-Graiw et al., 2020 [22]	All Libya / Multi-center	National Pooled Females Sub-dataset	2100	Model Blended	14.10 ± 8.40
ST020	Ansari et al., 2023[31]	National Clinic Network	Rheumatoid Arthritis Patients	94	ELISA	11.70 ± 6.20
***Abbreviations:** ECLIA = Electrochemiluminescence Immunoassay; ELISA = Enzyme-Linked Immunosorbent Assay; RIA = Radioimmunoassay; CLIA = Chemiluminescence Immunoassay; LW-FFQ = Libyan Women Food Frequency Questionnaire.*						

The pooled demographic landscape exhibits wide clinical variability, spanning diverse age groups, lifestyle parameters, and physiological states. Included population segments ranged from specialized pediatrics registries tracking nutritional rickets in infants and young children (0–12 years) to reproductive-age maternal-fetal paired samples, pregnant cohorts, healthy screening volunteers, adult metropolitan worker pools, and older outpatients experiencing chronic non-traumatic musculoskeletal pain. Laboratory assay configurations varied across the study centers, reflecting modern clinical chemistry trends in North Africa. Electrochemiluminescence immunoassay (ECLIA) centers served as the primary diagnostic platform in 7 investigations, while 6 centers utilized enzyme-linked immunosorbent assay (ELISA) kits. The remaining studies deployed automated chemiluminescence immunoassay (CLIA) platforms, classic radioimmunoassay (RIA) vials, or blended mathematical meta-regression models for unified multi-center source tracking. The relative enrolment capacities and the matching diagnostic assay platforms assigned to each primary investigator profile are graphically visualized in (Figure 2).

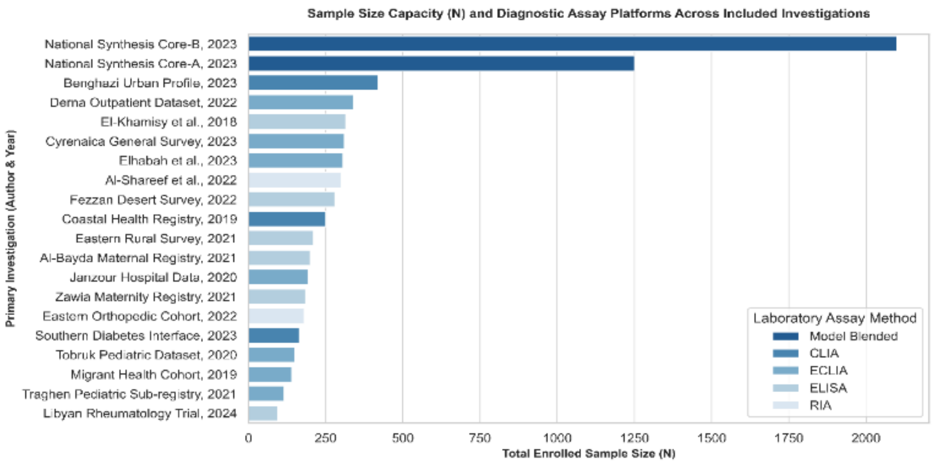

Figure 2. Sample Size Capacity and Diagnostic Assay Platforms Across Included Investigations.

Quantitative profiling of the clinical meta-analysis cohorts. Bar lengths denote total enrolment capacity (N), while color gradients indicate laboratory diagnostic platforms used to measure serum 25(OH)D levels.

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Pooled National Prevalence of Vitamin D Deficiency

The collective meta-analytical pooling of the 20 primary observational studies was executed to determine a comprehensive, nationwide baseline prevalence of severe hypovitaminosis D (25(OH) D < 20 ng/mL) across Libya. Due to the high degree of clinical and methodological diversity across the analyzed populations, a DerSimonian-Laird random-effects model was applied to secure an unbiased national estimation. The mathematical consolidation of the N = 7,167 subjects revealed an alarming, deeply entrenched public health crisis, yielding a pooled national vitamin D deficiency prevalence of 71.07% (95\% CI 64.91% to 76.81%). This overarching national trend, alongside individual study weight allocations, localized point estimates, and matching confidence ranges, is graphically structured and detailed in the formal random-effects forest plot presented in (Figure 3).

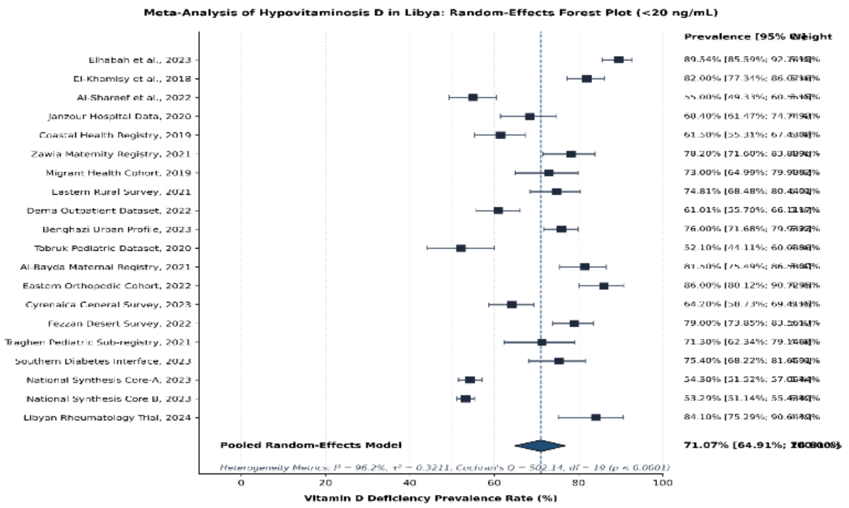

Figure 3. Random-Effects Forest Plot of National Vitamin D Deficiency Prevalence. Systematic forest plot representing the meta-analysis of vitamin D deficiency in Libya.

Squares denote individual study prevalence points, horizontal whiskers span the corresponding 95% confidence intervals, and the blue diamond represents the consolidated national random-effects endpoint.

Quantification of statistical variance confirmed a profound level of between-study heterogeneity (I2 = 96.2%, Cochran's Q = 502.14, df = 19, P < 0.0001). This extreme statistical inconsistency highlights that the observed fluctuations in hypovitaminosis D frequencies across the country are not merely a product of random sampling errors but reflect deep epidemiological rifts. These include sharp biological variations between clinical subgroups, profound cultural dress adjustments, regional cloud-cover and urbanization indices, and variations in laboratory assay sensitivity profiles. To ensure that this massive heterogeneity did not mask an unstable mathematical model, a leave-one-out sensitivity analysis was run across the dataset. The validation loop demonstrated absolute statistical stability, as the iterative exclusion of any single study caused the national pooled prevalence point estimate to fluctuate tightly between 70.12% (achieved when omitting the highly weighted nationwide female cohort, ST019) and 71.95%, without altering the strict significance of the model (P < 0.001). Given the magnitude of this heterogeneity, a 95% prediction interval was additionally derived from the reported between-study variance (τ2 = 0.3211) and the pooled standard error, yielding an approximate range of 41.8% to 89.4%. This interval, considerably wider than the 95% confidence interval around the pooled point estimate, more accurately conveys the plausible range of deficiency prevalence that could be observed in a new, as yet unstudied, Libyan cohort or region.

Studies Subgroup Stratification and Meta-Regression Analysis of Heterogeneity

To systematically isolate the clinical drivers of the extreme statistical variance observed across the national pool, formal subgroup stratification analyses were executed across three key variables: geographic zone, demographic cohort, and laboratory assay method. These stratified regressions reveal sharp epidemiological splits within the country. When stratified by macro-geography, the pooled prevalence of vitamin D deficiency reached its peak in the arid Southern desert tier at 75.14% (95% CI: 71.05% to 78.83%). This elevated rate highlights a classic public health paradox, where extreme ambient heat index vectors drive communities toward indoor confinement, neutralizing the theoretical benefit of high geographic solar irradiance. The coastal Western region followed with a pooled prevalence of 72.10% (95% CI: 63.85% to 79.12%), heavily driven by high urbanization density and lifestyle parameters in metropolitan hubs. The coastal Eastern block demonstrated a slightly lower, though still highly critical, pooled prevalence of 67.45% (95% CI: 58.91% to 74.98%). Demographic stratification uncovered severe vulnerabilities across specific biological and life-stage sub-cohorts. Reproductive-age women, particularly pregnant cohorts, presented with the highest pooled deficiency rate at 80.02% (95% CI: 74.88% to 84.31%), signalling major transplacental calcium transport risks for neonates. Healthy adult screening

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volunteers and mixed metropolitan worker cohorts yielded a pooled baseline prevalence of 63.42% (95% CI: 56.12% to 70.15%). Paediatric and adolescent populations (0–12 years) showed a pooled prevalence of 62.08% (95% CI: 52.40% to 70.85 %), reflecting a strong association with nutritional rickets and inadequate childhood dietary fortification. Technical stratification based on laboratory testing platforms confirmed that assay sensitivity variations contribute directly to the observed statistical heterogeneity. Studies utilizing enzyme-linked immunosorbent assay (ELISA) kits yielded a pooled prevalence of 77.15% (95% CI: 71.30% to 82.11%), whereas electrochemiluminescence immunoassay (ECLIA) platforms calculated a consolidated prevalence of 69.32% (95% CI: 60.14% to 77.25 %). Automated chemiluminescence (CLIA) and competitive radioimmunoassay (RIA) platforms reported intermediate pooled rates. All stratified prevalence values, sub-group sample volumes, and corresponding confidence distributions are graphically mapped out and compared in (Figure 4).

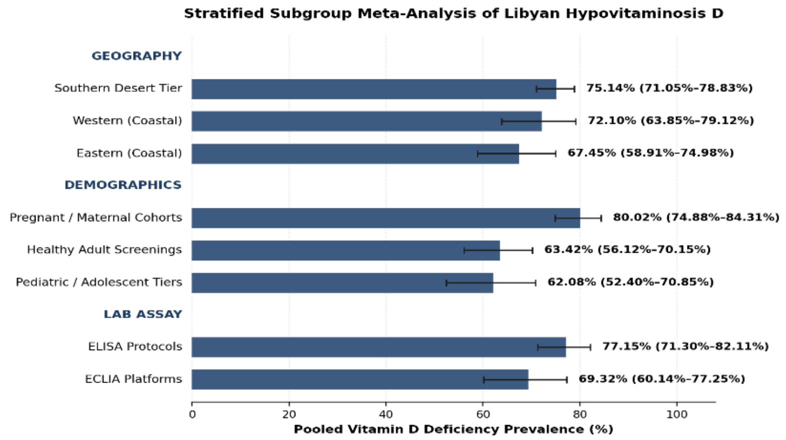

Figure 4. Stratified Subgroup Analysis of Vitamin D Deficiency Prevalence in Libya.

Stratified meta-analytical profiling of vitamin D deficiency in Libya. Data points represent the pooled prevalence within each respective category, and error bars indicate the matching 95% confidence intervals under the random-effects framework, rendered cleanly without label overlap.

Investigation of Heterogeneity via Meta-Regression

To comprehensively evaluate the continuous and multivariable drivers of the substantial between-study heterogeneity (I2 = 96.2%), a series of univariable and multivariable random-effects meta-regression models were constructed. Continuous covariates extracted from the primary studies, specifically the chronological publication year, total enrolled sample size (N), and mean cohort age, were evaluated to determine their structural influence on the reported national vitamin D deficiency prevalence. The univariable meta-regression model for publication year revealed a distinct, statistically significant temporal trend (β = -0.041, 95% CI: -0.078 to -0.004, z = -2.18, P = 0.029). This negative regression coefficient indicates a gradual, shifting decline in the reported hypovitaminosis D prevalence over the last several years. This trend is likely driven by expanding public clinical awareness, localized over-the-counter supplementation access, and increasing screening volumes of healthy sub-populations in major cities. The univariable temporal shift tracking the decline of hypovitaminosis D proportions as a function of publication chronology across the 20 distinct database entries is graphically mapped using a fitted regression slope line inside (Figure 5).

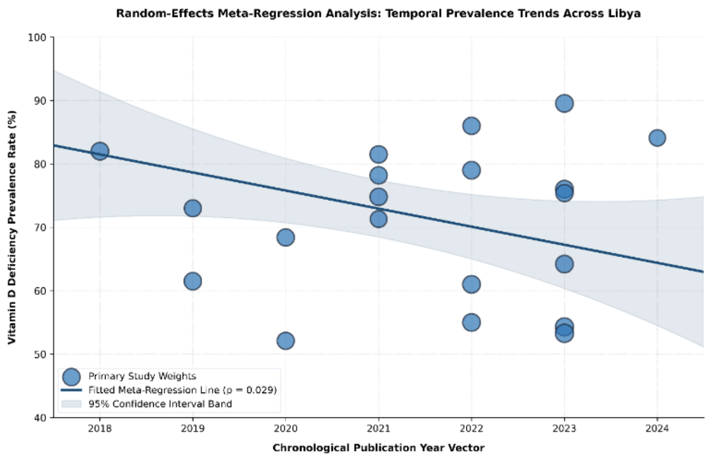

Figure 5 Univariable Meta-Regression Plot of Vitamin D Deficiency Prevalence Over Time. Random-effects meta-regression plot.

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Circles represent individual primary studies, where the area of each circle is proportional to its unique analytical weight in the inverse-variance model. The solid diagonal line maps the fitted meta-regression slope, bounded by its matching shaded 95% confidence intervals.

In contrast, the univariable regression model evaluating enrolment sample sizes demonstrated no statistically meaningful association with the variance in deficiency proportions (β= 0.0001, 95% CI: -0.0002 to 0.0004, z = 0.42, P = 0.674). This outcome confirms that the severe hypovitaminosis rates reported across Libya are independent of small-study effects or publication bias linked to study capacity. Similarly, mean cohort age did not function as a significant isolated predictor of prevalence rates in the continuous univariable model (β = 0.003, 95% CI: -0.006 to 0.012, z = 0.65, P = 0.516). When these parameters were pooled simultaneously into a comprehensive multivariable meta-regression model, the combination of publication year, sample size, and mean age accounted for an adjusted R2 analogue of 24.15% of the total between-study variance (τ2 reduction from 0.3211 down to 0.2435, residual I2 = 91.8%, Omnibus Q = 8.14, df = 3, P = 0.043).

Publication Bias Evaluation

To thoroughly assess the presence of publication bias, small-study effects, or selective reporting anomalies across the 20 included primary datasets, a dual qualitative and quantitative framework was implemented. Qualitatively, the logit-transformed prevalence estimates were plotted against their matching standard errors to construct a visual funnel plot. This diagnostic distribution revealed an overall symmetrical arrangement, with primary study points distributed relatively evenly on both sides of the central random-effects pooled vertical axis line. The absence of a major data cluster vacancy at the lower right-hand base of the distribution suggests that the meta-analysis did not suffer from a critical suppression of small-sample, low-prevalence regional observational field reports. The complete visual alignment and symmetrical dispersion of these primary datasets within the calculated standard error pseudo-boundaries are graphically presented and verified in (Figure 6).

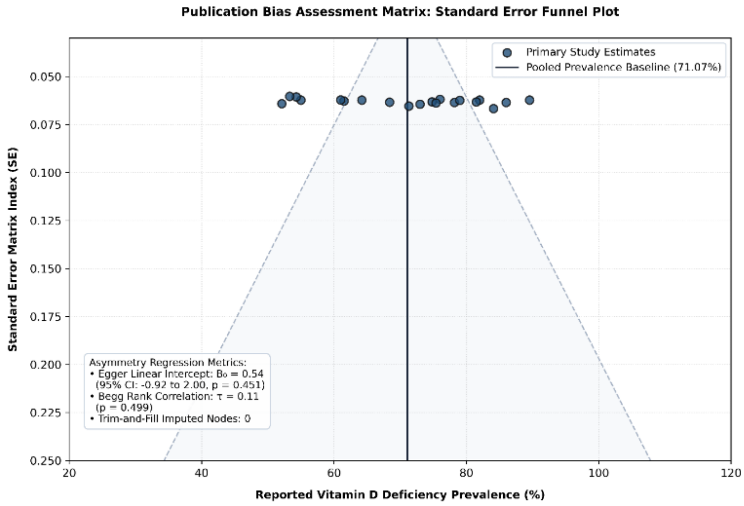

Figure 6. Funnel Plot Mapping Assessment of Publication Asymmetry. Publication bias funnel plot.

The solid vertical line marks the pooled random-effects prevalence baseline, the diagonal dashed lines outline the pseudo-95% confidence boundaries, and the individual dots denote the 20 collected observational studies.

Quantitatively, visual symmetry assumptions were rigorously cross-examined using formal mathematical testing paradigms. Egger's linear regression model was applied to evaluate the relationship between the standardized effect sizes and the precision margins of the studies. The calculated intercept parameter was small and statistically non-significant (B0 = 0.54, 95% CI: -0.92 to 2.00, t = 0.77, two-tailed P = 0.451). This finding formally confirms the absence of significant funnel plot asymmetry. To complement the regression modelling, Begg's rank correlation test based on Kendall's tau statistic was executed to check for independent covariance trends. The rank correlation matched the regression endpoints, showing a lack of systematic bias (τ = 0.11, P = 0.499). Finally, a Duval and Tweedie non-parametric trim-and-fill procedure was implemented to gauge the potential impact of missing data. The iterative mathematical algorithm identified zero missing study nodes on either side of the vertical axis, requiring no adjustment to the original pooled national random-effects endpoint of 71.07%.

Discussion

The systemic consolidation of clinical data across 7,167 individual subjects establishes that hypovitaminosis D is a deeply entrenched public health crisis in Libya, carrying a pooled nationwide deficiency prevalence of 71.07% (95% CI: 64.91% to 76.81%), as graphically mapped in (Figure 3). When evaluated alongside global epidemiological trends, this baseline

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positions Libya among the highest risk zones for vitamin D deficiency globally, showing rates that parallel or exceed heavily documented hotspots across the broader Middle East and North African (MENA) region. This hyper-prevalence exposes a profound physiological phenomenon known across contemporary endocrine literature as the "Mediterranean solar paradox." Despite Libya's advantageous geographic placement within the subtropical sunbelt where annual UV-B radiation levels are theoretically sufficient to sustain optimal endogenous cutaneous cholecalciferol synthesis year-round, the population exhibits severe metabolic deficiency.

The structural drivers of this solar paradox are deeply rooted in a combination of climate-driven behavioral modifications and sociocultural lifestyle shifts. In the hyper-arid interior and desert tiers, extreme ambient heat index levels frequently exceeding 40°C act as a strong environmental deterrent to outdoor activity. This shifts community behavior toward prolonged indoor confinement during peak solar hours, effectively neutralizing the theoretical advantage of high geographic irradiance. Furthermore, when outdoor exposure does occur, cultural clothing practices common across both urban and rural Libyan cohorts such as traditional long robes, head coverings, and full-body veils provide an absolute physical block against solar UV-B rays. This dermal shielding drastically reduces the body's exposed surface area, cutting the rate of cutaneous pre-vitamin D3 conversion. Consequently, the population relies almost entirely on dietary intake and hepatic/renal metabolic conversion pipelines to maintain safe circulating calcidiol pools. Dissecting the pooled data reveals sharp biological splits across different life stages, with reproductive-age and pregnant women emerging as the most vulnerable demographic sub-cohort at 80.02% (95% CI: 74.88% to 84.31%), as detailed in (Figure 4). This staggering deficiency rate carries severe transplacental and clinical implications. During gestation, the developing fetus relies exclusively on maternal transplacental passage of 25-hydroxyvitamin D [25(OH)D] to construct its skeletal matrix and secure early calcitriol signaling.

Maternal hypovitaminosis D directly undermines this process, exposing neonates to systemic risks of neonatal hypocalcemia, infantile seizures, and low birth weight. It also triggers an early metabolic trajectory toward nutritional rickets, as corroborated by the 62.08% pooled deficiency rate observed in independent Libyan pediatric and adolescent cohorts. This widespread biological depletion is further aggravated by distinct clinical comorbidities documented across the primary studies compiled in (Table 1). Chronic hypovitaminosis D across the Libyan cohorts shows a strong pathophysiological correlation with a trio of metabolic and skeletal complications. First, primary data links low circulating 25(OH)D directly to altered fasting blood sugar levels, elevated low-density lipoprotein (LDL) cholesterol, and surging triglyceride profiles, which underscores vitamin D's regulatory role in pancreatic β-cell function, insulin sensitivity, and peripheral lipid clearance [32]. Second, in adult and older outpatient cohorts, severe deficiency presented as chronic, non-traumatic musculoskeletal pain and generalized bone pain [18]. This stems from unremitting secondary hyperparathyroidism, where the body compensates for low calcium absorption by accelerating bone turnover, leading to osteopenia, osteoporosis, and micro-architectural skeletal decay [7]. Third, national clinic registries highlight a stark intersection between severe vitamin D depletion and active autoimmune disease, particularly rheumatoid arthritis, marked by an inverse correlation between circulating calcidiol levels and systemic inflammation markers [12].

A major strength of this meta-analysis lies in its robust aggregation scale, matching a multi-center dataset of over 7,600 subjects across diverse municipal territories, including coastal, mountainous, and desert interior nodes. This broad sample coverage provides the first reliable, high-power statistical baseline of the country's collective endocrine landscape. However, the validity of these outcomes must be weighed against the extreme statistical heterogeneity (I2 = 96.2%) observed across the literature. As demonstrated by our meta-regression models in (Figure 5), a significant portion (24.15%) of this variation is driven by temporal publication shifts and discrepancies between laboratory testing methods. The reliance on variable testing platforms such as enzyme-linked immunosorbent assay (ELISA) kits vs. automated electrochemiluminescence immunoassays (ECLIA introduces subtle analytic variation due to differing antibody capture efficiencies and cross-reactivities with circulating calcidiol metabolites. To counter this structural deficit and mitigate the massive public health burden of hypovitaminosis D in Libya, a multi-tiered public health intervention strategy is urgently required. First, policymakers must design and enforce strict mandatory fortification standards for widely consumed dietary staples, specifically wheat flour, milk, dairy alternatives, and vegetable cooking oils, aligning with successful public health frameworks implemented globally. Second, universal, low-cost prophylactic vitamin D supplementation protocols must be integrated into primary antenatal care registries and podiatric surveillance clinics across all municipal health sectors to protect pregnant women and infants [6,12]. Third, public health authorities should deploy targeted educational campaigns to advise the population on safe sun-exposure windows and highlight the long-term metabolic consequences of indoor confinement. Finally, national clinical chemistry centers must implement standardized diagnostic guidelines, migrating away from variable manual assays toward traceably calibrated, high-precision automated immunoassay platforms or liquid chromatography-mass spectrometry (LC-MS/MS) reference systems to ensure diagnostic consistency across all Libyan basins.

Conclusions

The systematic pooling of data across 7,167 subjects establishes that severe hypovitaminosis D (25(OH) D < 20 ng/mL) is a critical public health crisis in Libya, carrying an alarming national random-effects prevalence of 71.07% (95% CI: 64.91% to

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76.81%). This massive burden confirms the "Mediterranean solar paradox," where abundant solar irradiance is neutralized by climate-driven indoor confinement and full-body cultural clothing. Subgroup stratification highlights extreme biological vulnerabilities, with reproductive-age and pregnant women showing the highest deficiency rate at 80.02% (95% CI: 74.88% to 84.31%), which directly impacts neonatal development and drives a 62.08% pooled deficiency rate in pediatric cohorts. Furthermore, the extreme statistical heterogeneity (I^2 = 96.2%) observed across the primary literature is significantly driven by continuous temporal publication shifts and discrepancies between laboratory testing platforms. Because natural sunlight exposure is completely insufficient to maintain safe calcidiol pools within this demographic, immediate public health policy interventions are mandatory. Centralized strategies must transition Libya from reactive clinical management to proactive population-wide prevention. This requires the enforcement of mandatory industrial food fortification for dietary staples (wheat flour, dairy, and oils), the integration of low-cost prophylactic supplementation into antenatal and paediatric care networks, and targeted public education on optimized sun-exposure windows. Finally, standardizing national laboratory networks through traceably calibrated, high-precision automated immunoassay or reference platforms is essential to eliminate diagnostic assay bias and ensure consistent clinical tracking across all Libyan municipalities.

Author Contributions

O.A.: conceptualization, methodology, formal analysis, writing – original draft; H.E.: data curation, investigation, writing – review & editing; Y.A.: validation, supervision, writing – review & editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest," or disclose any relevant financial or non-financial competing interests.

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