Vitamin D Deficiencies among Tuberculosis Patients in Africa: A Systematic Review

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Content

Background

- Sun exposure as therapeutic approach to treat TB was used more than 100 years ago

- Vitamin D is a known
  - immunemodulator [Villamor, 2006]
  - improve **cell-mediated immunity** [Yang, et al., 1993]
  - phagocytic capacity of **macrophages** [Raubenheimer and Noffke, 2011].
  - increase the production of antimicrobial peptides such as, cathelicidin.

- Most (90%) of vitamin D is synthesized in the skin under the influence of ultraviolet sunlight [Mahmoud and Ali, 2014].

Objective

- Few community and facility based studies were conducted in Africa over the past to assess the **distribution** of VDD in TB patients and their causal effect relationship.

- These studies have given an **insight view** of the status of vitamin D in TB patients.

- However, there are three questions that need to be addressed
    1. Is VDD common in TB patients living in Africa?
    2. If yes, which level of deficiency is highly predominant?
    3. What are the predictor variables of VDD?

- Therefore, the present study was designed to address these three questions through a **comprehensive systematic review** of all articles published in peer reviewed journals.

- Background
- **Methods**
- Results
- Discussion
- Limitations of the analysis
- Conclusion
- Recommendation
- Acknowledgements

Methods

- *Data sources and search strategy*
  - PRISMA guidelines and checklists were used
  - Electronic search of Medline/PubMed, Web of Science, Scopus and Google Scholars was made to May 25, 2014.

- *Eligibility Criteria*
  - focused on studies reporting VDD among TB patients in Africa without restricting for age, sex, or ethnicity.
  - We included all original articles in English language published in peer reviewed journals.

Methods

- *Data extraction and processing*
  - author (s), publication year, country/ city, latitude, study type, sample size, TB cases, age, laboratory test, predictor variables and percentages of male, female and serum 25-OH-D <75, <50 and <25 nmol/L.

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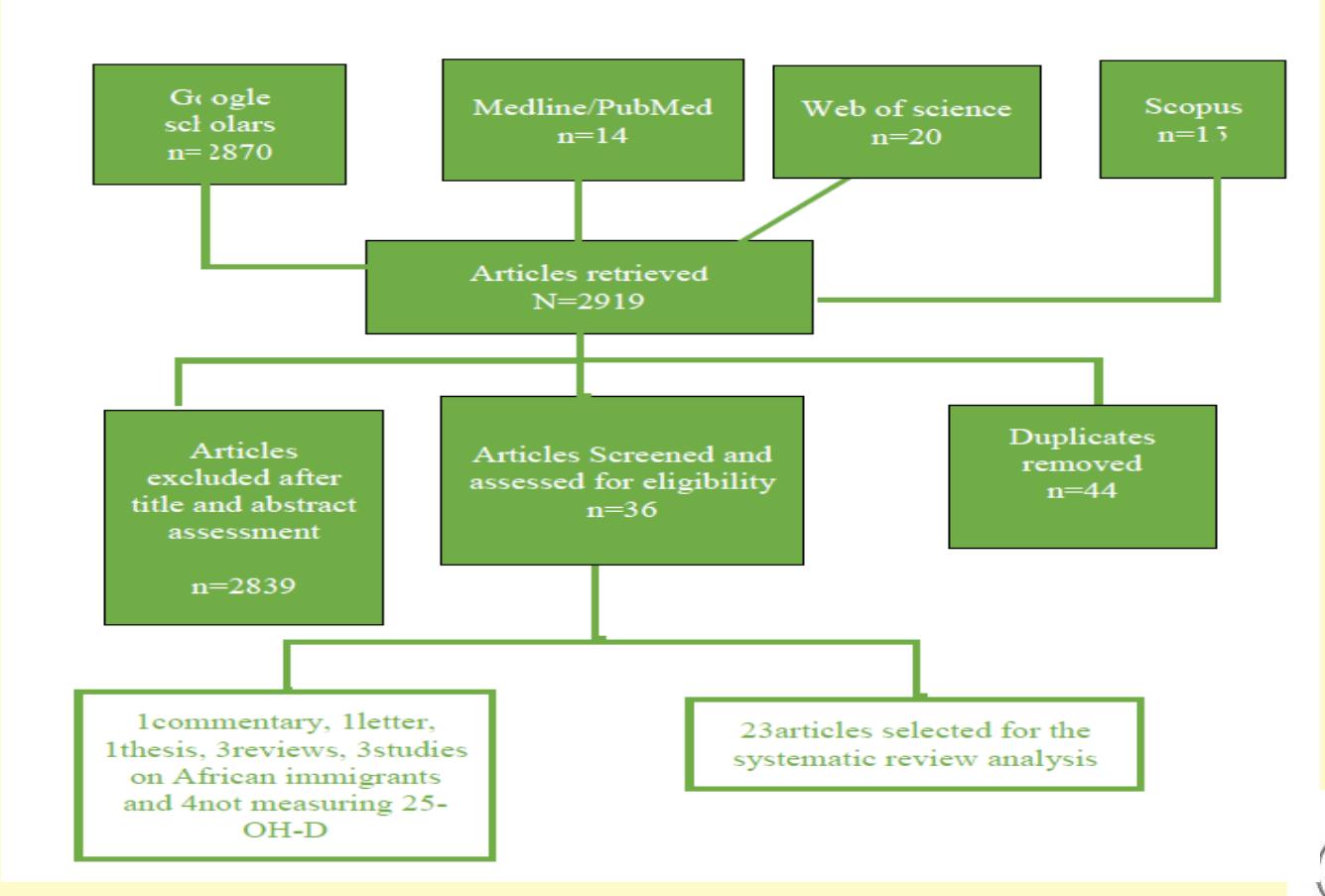
Results

- *Search results*



Results

- *Study characteristics*
  - Of the 23 studies,
    - 11 were done in Eastern Africa (Latitude 06$_{o}$50’S-10$_{o}$N),
    - 5 in Southern Africa (Latitude 13$_{o}$30’S-33$_{o}$S),
    - 4 in Western Africa (Latitude 06$_{o}$25’N-12$_{o}$N) and
    - 3 in Northern Africa (26$_{o}$34’N-36$_{o}$43’N).
  - Most of the studies were **cross sectional** and **prospective** type.
  - Considering all studies reviewed, 15 studies reported the vitamin D status in TB patients.

Result

- Laboratory tests.
  - 8 studies used immuno-assay,
  - 5 used HPLC,
  - 4 used LC-MS/MS
  - 6 used other tests

Results

- *Vitamin D deficiency*
  - Threshold level of 25-OH-D concentration was inconsistent
  - we summarized the definition of serum vitamin D status as follow: **sVDD** <25 nmol/L; **VDD** <50 nmol/L and **VDI** <75 nmol/L.
  - 22 studies in the population and 15 studies in TB patients reported the **prevalence** of **VDD** in the range of 1.2%-88.9%.
  - 20 studies in the population and 13 studies in TB patients reported the prevalence of **VDI** ranging between 17.3% and 96.3%
  - Considering the regions, the highest prevalence of **VDI** (74.5%-96.3%) and **VDD** (42%-88.9%) in TB patients were reported in Southern Africa.

Results

- *Predictor variables of vitamin D deficiency*
  - In the present study, 22 articles identified predictor variables associated with VDD.

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Discussion

- The relationship between vitamin D and TB may be mediated through the mechanisms of increased **cathelicidin** production and enhancement of the **capacity** of **macrophages**

- All the studies reported the prevalence of **VDD** up to **88.9%** and **VDI** to **96.3%**.

- The deficiency of **sunshine derived** vitamin in a **sunny** continent was not expectable. However, VDD and VDI were identified as common problem among TB patients in Africa. But, what are the predictors of these deficiencies in Africa?

Discussion

- *Predictors of vitamin D deficiencies*
  - *Lack of Sun exposure and inadequate diet intake*
    - Reported by almost all eligible studies
    - Only **brief daily sun exposure** is required to produce adequate vitamin D (Friis, et al., 2008)
    - Naturally, small number of foods contain vitamin D, including oily fish, liver, meat, egg yolk, and dairy products
    - Sundried mushroom is rich in ergocalcipherol (vitamin D2)

Discussion

- *Season*
  - An 8 year period study in South Africa showed the **highest** concentration of serum 25-OHD in **January** through **March** and **lowest** in **July** through **September** (56.8 vs. 30.7 nmol/L, respectively; P <0.001) [Martineau, et al., 2011].
  - A study conducted on reciprocal seasonal variation in TB notifications also indicated the **highest TB cases** in **October** through **December** (4,222 vs. 5,080; P <0.001) and the **lowest** in **April** through **June** [Martineau, et al., 2011].
- *Clothing, Comorbidities and Low BMI*
  - Studies conducted in Eastern, Western and Northern Africa identified **clothing** as predictor variable of VDD
  - **Comorbidities** with TB, HIV, Pneumonia, Oral thrush and Heart failure were identified as predictor variables of VDI in Eastern, Western and Southern Africa.
  - a positive relationship between **BMI** (<18.5) and VDD was ident

Discussion

- *Use of ART and anti-TB drugs*
  - Studies done in South Africa and Uganda demonstrated that the use of **ART** and **anti TB drugs** decreases 25-OH-D concentration
  - These drugs potentially stimulate **cytochrome P450 enzymes** which can catabolize vitamin D [Bolland, et al., 2008].
- *Age, Gender and Marital status*
  - Increasing age was independently associated with VDD
    - This is justified by the inverse relationship between **age** and **previtamin D3** concentration in the epidermis [MacLaughin and Holick, 1985].
  - **Gender** was also identified as a significant risk factor of VDD in the Middle East and North African (MENA) [El-Rassi, et al., 2009].
  - **Single patients** have lower serum 25-OH-D concentration as compared to married patients. This is more likely due to behavioural differences leading to work-related differences in sun exposure [Friis , et al., 2008].

Discussion

- *Skin pigmentation, Religion and Ethnicity*
  - Skin pigmentation was reported as significant predictor variable of VDD in Eastern and Northern Africa, respectively [Feleke, et al., 199; Djennane, et al., 2014].
    - as **melanin** efficiently absorbs UVB radiation, dark skin persons require 3 to 4 times longer sun exposure [Clemens, et al., 1982]
  - Studies done in Western Africa also indicated that **religion** and **ethnicity** were predictor variables of VDD.
    - Glew et al. described that being **Muslim**, the women do not derive much benefit from sunlight [Glew, et al., 2010].
- *Socio-economy, Time spent outdoors and Money spent on food*
  - *Were also attributed to VDD and VDI*

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Limitation of the analysis

- Lack of representative studies from central Africa

- Heterogeneity in study designs, sample sizes, and laboratory tests.

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Conclusion

- VDD and VDI were predominantly occurring among TB patients in Africa.

- Understanding the existence of the problems with their predictor variables enable us to further **question** about:
    - what is the association between vitamin D status and TB? And
    - what should be done to address the problem?

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Recommendation

- To address VDD and VDI, the options are:
  - Vitamin D supplementation, food fortification, diet diversification and bio-fortification, but these are economically less feasible.
  - Could we suggest **sunshine for free**?

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THANK YOU SO MUCH
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