

Are salivary cytokines biomarkers in oncological and infectiuos diseases?

- A systematic review

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Background

- Human saliva is a complex fluid containing
 - proteins (including cytokines)
 - organic and inorganic substances
 - **important for oral health**
- Saliva can be used as diagnostic tool:
 - low-cost, non-invasive, easy collection

Aim

- To review the **potential use** of salivary cytokines as diagnostic tool in oral and acute systemic diseases focusing on oncological and infectious conditions

Methods

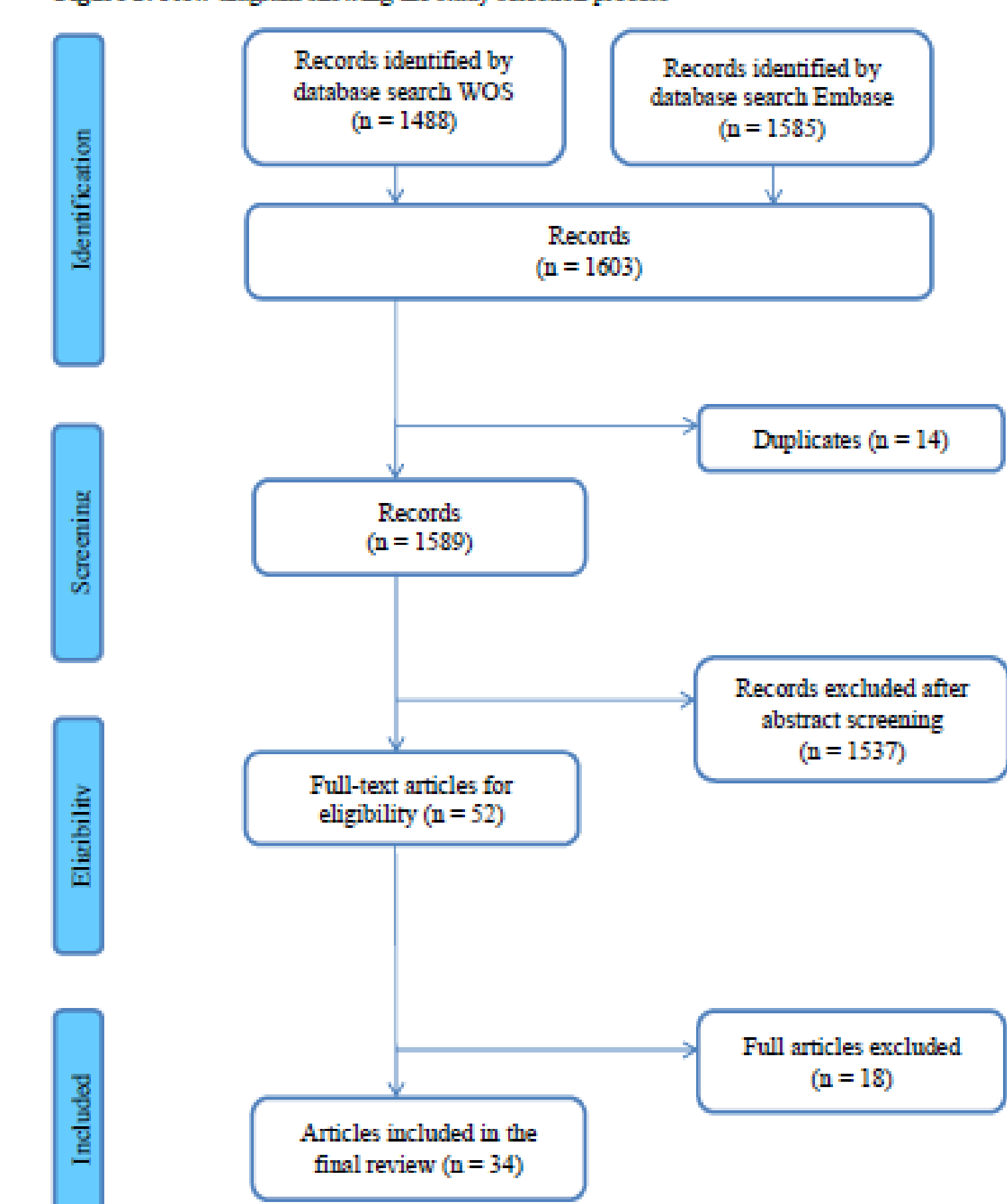
Study type

- Systematic review according to PRSIMA (**Figure 1**)
- Original papers published between January 1998 and December 2019

Variables

- Target population: adults/pediatric
- Mean age
- Type of saliva sample for cytokine analysis
- Type of applied assay
- Main findings

Figure 1: Flow diagram showing the study selection process



Results

- 1603 Publications were identified
- 34 Studies were included from 13 different countries
- 8 Studies only in children
- 24 Studies in adults only

Summary of analyzed cytokines in > 2 studies

First author	Year of Publication	Time point	IL-1	IL-1a	IL-1b	IL-1ra	IL-2	IL-4	IL-5	IL-6	IL-8	IL-10	IL-12	IL-13	IL-15	IL-17a	IL-21	IL-33	TNF-α	TNF-β	IFN-γ	VEGF-α
Krzaczek	2019	T0																				
Pels	2015	T0																				
		T1																				
		T2																				
Morales-Rojas	2011	T0																				
		T1																				
		T2																				
Fall-Dickson	2007	T0																				
		T1																				
Resende	2010	T0																				
		T1																				
Resende	2013	T0																				
		T1																				
Koizumi	2018	T0																				
Spear	2005	T0																				
Vastardis	2003	T0																				
Black	2000	T0																				
Jacobs	2016	T0																				
		T1																				
		T2 *																				
Jacobs	2016	T0																				
		T1																				
		T2																				
Bartolini	2018	T0																				
Sharma	2017	T0																				
		T1																				
Coguin	2015	T0																				
Menon	2016	T0																				
		T1																				
Garnowicz	2012	T0																				
Wu	2018	T0																				
Lee	2018	T0																				
		T1																				
Teles	2009	T0																				
		T1																				
		T2																				
		T3																				
		T4																				
		T5																				
Santos	2016	T0																				
Liskmann	2006	T0																				
Leigh	2002	T0																				
Deepthi	2019	T0																				
Lee	2018	T1																				
Zhang	2016	T0																				
Polz-Dacewicz	2016	T0																				
		T1																				
		T2																				
Russo	2016	T0																				
		T1																				
Bossi	2016	T0																				
		T1																				
		T2																				
Korostoff	2011	T0																				
Sharma	2011	T0																				
Katakura	2007	T0																				
Rhodes	2005	T0																				

Not analysed
Slightly elevated
Elevated
Slightly decreased
Decreased
No changes

Results

- Cytokine analysis (ELISA or xMAP)
 - n= 24 in saliva only
 - n = 8 in saliva and blood
 - n = 1 saliva and buccal epithelia
 - n = 1 saliva, blood and tissue
- In 30 studies **unstimulated saliva** was used
- The **most investigated cytokines** were
 - IL-6 (67%)
 - Tumor necrosis factor (TNF)-α (44%)
 - IL-10 (41%)

Discussion

- IL-1β, IL-2, IL-6 and TNF-α are associated with severity of **oral mucosal tissue damage**
 - early therapeutic intervention before quality of life of pts is impaired
- IL-10 was associated **with GvHD**, IL-1β might predicted GvHD development
- IFN-γ concentrations correlate with **HIV infection** and oral complications
- IL-1α, IL-1β, IL-6, IL-8 and TNF-α levels were associated with **oral dysplasia or cancer**

Limitations

- Heterogenity of studies (different collection methods, time of collection)
- Not considered in the analyzed studies the influence of:
 - age
 - smoking
 - dietary composition
 - hygiene standards

Conclusions

Saliva interesting biological fluid
useful in children and in countries with limited resources
for diagnosing and monitoring of oral and systemic diseases