



# A Systematic Review of the Zinc Concentrations in the Prostate Fluid of Normal and Inflamed Gland

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## Abstract

**Background and objective:** the prostate gland is subject to various disorders and of them chronic prostatitis (CP) is a complex disease. Various studies indicate some discrepancies regarding zinc (Zn) levels in prostatic fluid of normal and inflamed glands. The present study evaluated by systematic analysis the published data for Zn levels analyzed in expressed prostatic fluid (EPF) of normal and inflamed glands. **Methods:** The present systematic analysis included 25 studies, all of which were published in the years from 1961 to 2018 and selected by searching the databases Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science. The articles were analyzed and “Median of Means” and “Range of Means” were used to examine heterogeneity of Zn concentrations in two groups of subjects – apparently healthy men “N” and patients with prostatitis “P”. Moreover, using the ratios of prostatic fluid Zn in “P” group to prostatic fluid Zn in “N” group (ZnP/ZnN) obtained (or calculated by us) in the reviewed studies, “Median of Means” and “Range of Means” for these ratios were found. The objective analysis was performed on data from the 25 studies, with total 285 subjects in “P” group and more than 900 subjects in “N” group. **Results:** The range of means of Zn concentration reported in the literature for normal EPF varies widely from 47.1 mg/L to 825 mg/L with median of means 501 mg/L. The range of means of Zn concentration for EPF of untreated prostatitis varies also widely from 56 mg/L to 491 mg/L, with median of means 268 mg/L. Thus, the obtained median of means for Zn concentration in normal human prostatic fluid is about two times higher than median of mean values of the element content in EPF of inflamed prostate. In other words, the analysis of 25 studies with discordant data regarding prostatic fluid concentration of Zn demonstrated that there is a significantly diminished concentration of Zn in EPF of patients with prostatitis compared to controls. **Conclusion:** There is a significant relationship between lowered Zn concentrations in prostatic fluid and prostatitis, but because of small sample size and high data heterogeneity, we recommend other primary studies.

**Keywords:** Prostate, prostatitis, expressed prostatic fluid, trace elements, zinc

## Introduction

The prostate gland is subject to various disorders and of them chronic prostatitis (CP) is a complex disease. CP causes a range of symptoms including pain, urinary problems, such as urgency and frequency, reduced quality of life and sexual dysfunction<sup>[1-2]</sup>. Accounting for more than 90% of urological outpatient cases seen, CP remains one of the most common urologic disorders in men younger than 50 years old<sup>[3]</sup>. Etiology of CP is not fully understood and treatment is frequently unsuccessful<sup>[1-3]</sup>. Fragmentary epidemiological evidence indicates that risk factors such as infection, autoimmunity, inflammation, excessive amounts of tumor-related proteins, imbalance of hormones and nutrition-related variables, including Zn and some other trace elements (TEs) as micronutrients, may be associated with CP<sup>[4]</sup>.

In our previous studies the significant involvement of Zn, Ca, Mg, Rb and some other TEs in the function of the prostate was found<sup>[5-15]</sup>. Moreover, it was demonstrated that the changes of Zn content and levels of Zn/TE ratio in the prostate tissue can be used as biomarkers of prostate disorders<sup>[16-25]</sup>.

One of the main functions of the prostate gland is the production of prostatic fluid<sup>[26]</sup>. It contains a high concentration of Zn and elevated levels of Ca, Mg, Rb, and some other TEs, in comparison with levels in serum and other human body fluids. The first finding of remarkably high levels of Zn in human expressed prostatic fluid (EPF) was reported in the early 1960s<sup>[27]</sup>. After analyzing EPF expressed from the prostates of 8 apparently healthy men, aged 25-55 years, it was found that Zn concentrations varied from 300 to 730 mg/L. After this finding several investigators suggested that the measurement of Zn levels in EPF may be useful as a marker of abnormal prostate secretory function<sup>[28,29]</sup>. This suggestion promoted more detailed studies of the Zn concentrations in the EPF of healthy subjects and in those with different prostatic diseases, including CP<sup>[29,30]</sup>.

For humans, Zn is an essential nutritional TE, especially in terms of proteins and nucleic acids metabolism. It is required for the catalytic activity of at least 300 enzymes, and is involved in the human immune system, in tissue repair, and in DNA syntheses. There are a lot of data on the subject. For example its role in cell immunity and as an antioxidant has recently been reviewed<sup>[31-35]</sup>.

However, the exact role of Zn in normal and pathophysiology of the prostate is until now unknown.

The effects of TEs are related to concentration and recorded observations range from a deficiency state, to function as biologically essential components, to an unbalance when excess of one element interferes with the function of another, to pharmacologically active concentrations, and finally to toxic and even life-threatening concentrations<sup>[36,37]</sup>. Oxidative stress has significant involvement in the pathogenesis of CP<sup>[38]</sup>. Oxidative stress is a result of the imbalance between reactive oxygen species and antioxidants, including Zn and some other TE, in the body that can cause tissue and organ damage. In this context, the role in prostate disorders has been associated with non-adequate Zn content in tissues and fluid of the gland for a long time<sup>[34,36-40]</sup>.

Several studies have reported the Zn content in EPF of normal and inflamed gland<sup>[29,30,41-61]</sup>. But the findings of various studies indicate some discrepancies. One researcher has demonstrated a great decrease (almost 10 times) of Zn concentration in EPF of patients with CP compared to controls<sup>[56]</sup>, while others have not found the statistically significant effect<sup>[29,30,61]</sup>. Thus, further investigation has been considered necessary to provide clearer hypothesis about the role of Zn in CP.

The present study addresses the significance of prostatic fluid Zn levels in CP. Therefore, we systematically reviewed the available literature and performed a statistical analysis to evaluate the effect of inflammation on prostatic fluid Zn concentration, which may shed valuable insight into the diagnosis of CP.

## Materials and Methods

### Data sources and search strategy

Aiming at finding the most relevant articles for this review, a thorough comprehensive web search was conducted from Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science databases between 1961 to November 2019, using the key words: prostatitis, trace elements, Zn concentration, expressed prostatic fluid, and their combination. For example, the search terms for Zn concentration were: ‘Zn concentration’, ‘Zn content’, ‘Zn level’, ‘prostatic fluid Zn’ and ‘Zn of expressed prostatic fluid’, while those for prostatitis were: ‘chronic prostatitis’, ‘acute prostatitis’, and ‘prostate inflammation’. The language was not restricted. The titles from the search results were evaluated closely and determined to be acceptable for potential inclusion criteria. Also, references from the selected articles were examined as further search tools. Relevant studies noted in the reference lists of each selected article were also evaluated for inclusion.

**Table 1: Reference data of Zn concentration in normal human prostatic fluid (group “N”)**

Reference	Method	n	Age, years M(Range)	Samples preparing	Zn, mg/L	
					M±SD (Med)	Range
Birnbaum et al 1961 <sup>[41]</sup>	XRF	-	-	Intact	490	-
Mackenzie et al 1962 <sup>[42]</sup>	XRF	8	37(25-55)	Intact	490±130	265-666
Burgos, 1974 <sup>[43]</sup>	-	-	-	-	47.1	-
Marmar et al 1975 <sup>[44]</sup>	AAS	33	-	AD	451±215	-
Anderson & Fair, 1976 <sup>[45]</sup>	AAS	15	50(30-74)	AD	352±190	-
Fair et al 1976 <sup>[46]</sup>	AAS	49	52(24-76)	AD	455±208	150-1000
Paz et al 1977 <sup>[47]</sup>	AAS	53	-	AD	299±202	-
Fair & Cordonnier 1978 <sup>[48]</sup>	AAS	63	52(24-76)	AD	455±208	-
Homonnai et al 1978 <sup>[49]</sup>	AAS	12	-	AD	335±45	-
Marmar et al 1980 <sup>[50]</sup>	AAS	33	-	AD	451±215	-
Zaichick et al 1981 <sup>[29]</sup>	EDXRF	15	-	Intact	580±183	-
Zaneveld & Tauber 1981 <sup>[51]</sup>	-	-	-	-	50.3	-

### Eligibility criteria

Inclusion criteria: Studies were included if patients met the diagnostic criteria of prostatitis. The controls were healthy human males with no history or evidence of andrologia or urologic disease. Zinc was detected in samples of EPF.

Exclusion criteria: Studies were excluded if they were case reports. Studies involving patients with prostatitis that were undergoing Zn supplementation therapy were also excluded.

### Data extraction

A standard extraction of data was applied, and the following available variables were extracted from each paper for two groups of subjects with normal “N” and inflamed “P” prostate: method of Zn determination, number and age of health persons and patients, samples preparing, means and medians of Zn concentrations, standard deviations of means, range of Zn concentrations, and statistical difference of means. Abstracts and full articles were reviewed independently by two of the authors, and if the results were different, papers were checked jointly until the differences were resolved.

### Statistical analysis

Studies were combined based on means of Zn concentrations in EPF. The articles were analyzed and “Median of Means” and “Range of Means” were used to examine heterogeneity of Zn concentrations in two groups of subjects – “N” and “P”. Moreover, using the ratios of prostatic fluid Zn in “P” group to prostatic fluid Zn in “N” group (ZnP/ZnN) obtained (or calculated by us) in the reviewed studies, “Median of Means” and “Range of Means” for these ratios were also found. The objective analysis was performed on data from the 25 studies, with total 285 subjects in “P” group and more than 900 subjects in “N” group. In addition, two subgroups of data from group “N” were used to evaluate the difference between results obtained by destructive and non-destructive analytical methods.

## Results

A total of 1885 unduplicated studies were identified. Among them 25 studies were ultimately selected according to eligibility criteria, including 25 studies that investigated Zn concentrations in EPF of normal prostate (Table 1) and 11 studies that investigated Zn concentrations in EPF of both normal and inflamed prostate (Table 2). After discussion, all reviewers were in agreement to include all 25 papers.

Kavanagh et al 1982 <sup>[52]</sup>	AAS	35	49.2	AD	580	-
Kavanagh 1983 <sup>[53]</sup>	AAS	152	-	AD	595±222	52-1308
Zaichick et al 1996 <sup>[30]</sup>	EDXRF	22	49(22-75)	Intact	590±210	291-1118
Mo et al 2000 <sup>[54]</sup>	ICPAES	25	57.4±6.8	AD	305	243-379
Cai et al. 2002* <sup>[55]</sup>	AAS	22	-	AD	220±85	-
Gómez et al 2007 <sup>[56]</sup>	AAS	10	44(40-62)	AD	519±374	131-1242
Costello & Franklin 2009 <sup>[57]</sup>	EDXRF	24	-	Intact	588	-
Zhuang et al. 2009* <sup>[55]</sup>	AAS	20	-	AD	802±39	-
He et al. 2013* <sup>[55]</sup>	AAS	40	-	AD	825±71	-
Zaichick & Zaichick 2018 <sup>[58]</sup>	EDXRF	41	18-82	Intact	573±202 (552)	253-948
		13	28(18-40)	Intact	501±47	-
		38	59(41-82)	Intact	598±34	-
Zaichick & Zaichick 2018 <sup>[59]</sup>	EDXRF	42	31-75	Intact	559±204(549)	253-948
Zaichick & Zaichick 2018 <sup>[60]</sup>	EDXRF	38	41-82	Intact	598±207(560)	253-948
Zaichick & Zaichick 2018 <sup>[61]</sup>	EDXRF	38	41-82	Intact	598±207(560)	253-948
Median of means, mg/L		501				
Range of means (M <sub>min</sub> - M <sub>max</sub> ), mg/L		47.1 - 825				
Ratio M <sub>max</sub> /M <sub>min</sub>		(825/47.1)=17.5				

\* Data of Chinese researches taken from the review Cui et al 2015

M – arithmetic mean, SD – standard deviation of mean, Med – median, XRF - X-ray fluorescence, AAS - atomic absorption spectrophotometry, EDXRF - energy dispersive X-ray fluorescence, ICPAES - inductively coupled plasma atomic emission spectrometry, AD – acid digestion

Tables 1 and 2 summarize general data from the 25 studies. The retrieved studies involved 285 patients with prostatitis and more than 900 normal controls. The ages of subjects in “N” group were available for 14 studies and ranged from 18–82 years. The ages of subjects in “P” group were available for 5 studies and ranged from 25–72 years. The mean ages of subjects in the control and patient groups were available for 10 and 4 studies, respectively. The information about analytical method was available for 23 studies. Fourteen studies determined Zn concentration by the destructive

analytical methods: thirteen using AAS (atomic absorption spectrophotometry) and one using ICPAES (inductively coupled plasma atomic emission spectrometry). Nine studies detected Zn concentration in EPF by the non-destructive analytical methods, such as X-ray fluorescence analysis (XRF, 2 studies) and energy dispersive X-ray fluorescence analysis (EDXRF, 7 studies). Table 3 and 4 present data of Zn concentration in EPF of normal prostates obtained by the destructive and non-destructive analytical methods, respectively.

**Table 2: Reference data of Zn concentration in human prostatic fluid of normal (N) and inflamed (P) gland**

Reference	Method	n	Age, years M(Range)	Group “N” or “P”	Zn, mg/L M±SD	Zn <sub>P</sub> /Zn <sub>N</sub>	
Anderson&Fair, 1976 <sup>[45]</sup>	AAS	15	50(30-74)	N	352±190+	0.341	
		13	51(31-67)	P	120±90		
Fair et al 1976 <sup>[46]</sup>	AAS	91	52(24-76)	N	455±208+	0.319	
		15	-	P	145±62		
Fair&Cordonnier 1978 <sup>[48]</sup>	AAS	63	52(24-76)	N	455±208+	0.264	
		10	54(37-60)	P	120±101		
Zaichick et al 1981 <sup>[29]</sup>	EDXRF	15	-	N	580±183	0.676	
		18	-	P	392±284		
Kavanagh et al 1982 <sup>[52]</sup>	AAS	35	49.2	N	580+	0.153	
		29	49.4	P	88.9		
Zaichick et al 1996 <sup>[30]</sup>	EDXRF	22	49(22-75)	N	590±210	0.771	
		28	49(25-72)	P	455±317		
Cai et al. 2002* <sup>[55]</sup>	AAS	22	-	N	220±85+	0.700	
		30	-	P	154±90		
Gómez et al 2007 <sup>[56]</sup>	AAS	10	44(40-62)	N	519±374+	0.108	
		10	51(47-54)	P	56±24		
Zhuang et al. 2009* <sup>[55]</sup>	AAS	20	-	N	802±39+	0.612	
		52	-	P	491±46		
He et al. 2013* <sup>[55]</sup>	AAS	40	-	N	825±71+	0.593	
		47	-	P	489±49		
Zaichick&Zaichick 2018 <sup>[61]</sup>	EDXRF	42	31-75	N	559±204+	0.683	
		33	37-65	P	382±275		
Group “N”	Median of Means (mg/L)					559	
	Range of Means(mg/L)					220-825	
Group “P”	Median of Means (mg/L)					268	
	Range of Means (mg/L)					56-491	
Ratio Zn <sub>P</sub> /Zn <sub>N</sub>	Median of Means					0.593	

	Range of Means	0.108-0.771
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\* Data of Chinese researches taken from the review Cui et al 2015

+ Statistically significant differences between group "N" and "P"

M – arithmetic mean, SD – standard deviation of mean, AAS - atomic absorption spectrophotometry, EDXRF - energy dispersive X-ray fluorescence.

## Discussion

Samples of EPF are much more available for study than prostate tissue and can be obtained without damaging the prostate gland. Information about Zn concentrations in prostatic fluid in different prostatic diseases is of obvious interest, not only to more profoundly understand the etiology and pathogenesis of prostatic diseases, but also for their diagnosis, including prostatitis<sup>[29,30,55,59-61]</sup>. Thus, it dictates a need in reliable values for the Zn concentrations in the EPF of apparently healthy subjects ranging from young adult males to elderly persons, as well as in the EPF of patients with prostatitis.

The range of means of Zn concentration reported in the literature for normal EPF varies widely from 47.1 mg/L<sup>[43]</sup> to 825 mg/L<sup>[55]</sup> with median of means 501 mg/L (Table 1).

In present study, 11 articles studied the effect of prostate inflammation on the Zn concentration of EPF (Table 2). All of the 11 articles studied the impact of inflammation on Zn concentration in EPF reported that there was a decrease of Zn level. In nine of the 11 articles were found that the decrease of Zn level was statistical significant and only two studies showed the relatively small and non-statistical significant decrease<sup>[29,30]</sup>. In two studies conducted by Kavanagh et al.<sup>[52]</sup> and Gómez et al.<sup>[56]</sup>, it was observed that means of Zn concentration in EPF of inflamed prostates were almost 7 and 9 times, respectively, lower than in control group. However, in other studies the difference between patients with prostatitis and normal controls was lower and did not exceed 23-74%.

The range of means of Zn concentration reported in these 11 articles for normal EPF varies from 220 mg/L to 825 mg/L<sup>[55]</sup>, with median of means 559 mg/L (Table 2). However, the range of means of Zn concentration for EPF of untreated prostatitis varies widely from 56 mg/L<sup>[56]</sup> to 491 mg/L<sup>[55]</sup>, with median of means 268 mg/L (Table 2). Thus, the obtained median of means for Zn concentration in normal human prostatic fluid is about 2 times lower than median of mean values of the element content in prostatic fluid of inflamed prostate. In other words, the analysis of 11 studies with discordant data regarding prostatic fluid concentration of Zn demonstrated that there is a significantly diminished concentration of Zn in EPF of patients with prostatitis compared to controls. It is, therefore, reasonable to assume that Zn levels in EPF can reflect the role of this metal in the prostatitis etiology.

As indicated above, the range of means of Zn concentration reported in the literature for normal EPF and for EPF of untreated inflamed prostate varies widely. This can be explained by a dependence of Zn content on many factors, including age, ethnicity, mass of the gland, and others. Not all these factors were strictly controlled in cited studies. However, published data allowed us to estimate the effect of age at Zn concentration in EPF of normal prostate. In one study a significant increase in Zn concentration with increasing of age was shown by the Pearson's

coefficient of correlation between age and Zn concentration in EPF<sup>[58]</sup>. According this study Zn concentration in EPF of apparently healthy men aged 41-82 years was about 20% higher than in age from 18 to 40 years. But this finding does not agree with other published data. For example, in the first quantitative XRF analysis of Zn concentration in EPF of 8 apparently healthy men aged 25-55 years no significant variation with age was recognized, in spite of no any statistical treatment of results was done in this investigation<sup>[42]</sup>. Fair and Cordonnier<sup>[48]</sup> did not find any changes in the metal level with age using AAS for Zn measurement in EPF specimens obtained from 63 normal male subjects in age from 24 to 76 years. The conclusion was followed from the level of differences between the mean Zn results for three age groups evaluated by parametric Student's t-test. Additionally, Zn, concentration in prostatic fluid showed no age relationship in the study of Kavanagh et al.<sup>[52]</sup> when 35 specimens obtained from normal male subjects in age from 15 to 85 years were measured by AAS and the Pearson correlation between age and Zn concentration was used. It is, therefore, reasonable to assume that Zn level in EPF do not change with age or, at least, slightly increase in age above 40 years.

Another and, in our opinion, leading cause of inter-observer variability was insufficient quality control of results in these studies. In many reported papers such destructive analytical methods as AAS and ICP-AES were used. These methods need in an acid digestion of samples under high temperature. There is evidence that by use of these methods some quantities of TEs, including Zn, are lost as a result of this treatment<sup>[62-64]</sup>. On the other hand, TEs of chemicals used for the acid digestion can contaminate the EPF samples. XRF and, particularly, EDXRF is a fully instrumental and non-destructive method because a drop of EPF is investigated without requiring any sample pretreatment or its consumption<sup>[65]</sup>.

In present study, in 14 articles Zn concentration in EPF samples was determined by the destructive analytical methods (13 articles - AAS and 1 articles – ICP-AES) and in 9 articles non-destructive analytical methods were used for this purpose (2 articles – XRF and 7 articles – EDXRF). Thus, published data allowed us to estimate the effect of acid digestion on the results of Zn determination in EPF on normal prostates (Tables 3 and 4). In articles with destructive analytical methods the range of means for Zn concentration in EPF of normal prostates varied from 220 mg/L to 825 mg/L (ratio  $M_{max}/M_{min} = 3.75$ ), with median of means 453 mg/L (Table 3). The articles with nondestructive analytical methods have the rather narrow range of means for Zn concentration in EPF of normal prostates from 490 mg/L to 598 mg/L (ratio  $M_{max}/M_{min} = 1.22$ ), with median of means 580 mg/L. Thus, median of means for Zn concentration in EPF of normal prostates obtained by destructive analytical methods is 22% lower than that obtained by nondestructive methods. It is, therefore, reasonable to conclude that the choice of analytical method and quality control of results are very important factors for using the Zn concentration in EPF as biomarker of prostate diseases.

**Table 3: Reference data of Zn concentration in normal prostatic fluid investigated by destructive AAS and ICP-AES methods**

Reference	Method	n	Age, years M(Range)	Zn, mg/L M±SD
Marmar et al 1975 <sup>[44]</sup>	AAS	33	-	451±215



Anderson&Fair, 1976 <sup>[45]</sup>	AAS	15	50(30-74)	352±190
Fair et al 1976 <sup>[46]</sup>	AAS	49	52(24-76)	455±208
Paz et al 1977 <sup>[47]</sup>	AAS	53	-	299±202
Fair&Cordonnier 1978 <sup>[48]</sup>	AAS	63	52(24-76)	455±208
Homonnai et al 1978 <sup>[49]</sup>	AAS	12	-	335±45
Marmar et al 1980 <sup>[50]</sup>	AAS	33	-	451±215
Kavanagh et al 1982 <sup>[52]</sup>	AAS	35	49.2	580
Kavanagh 1983 <sup>[53]</sup>	AAS	152	-	595±222
Mo et al 2000 <sup>[54]</sup>	ICP-AES	25	57.4±6.8	305
Cai et al. 2002* <sup>[55]</sup>	AAS	22	-	220±85
Gómez et al 2007 <sup>[56]</sup>	AAS	10	44(40-62)	519±374
Zhuang et al. 2009* <sup>[55]</sup>	AAS	20	-	802±39
He et al. 2013* <sup>[55]</sup>	AAS	40	-	825±71
Median of means, mg/L	453			
Range of means (M <sub>min</sub> - M <sub>max</sub> ), mg/L	220 - 825			
Ratio M <sub>max</sub> /M <sub>min</sub>	(825/220)=3.75			

\* Data of Chinese researches taken from the review Cui et al 2015

M-arithmetic mean, SD – standard deviation of mean, AAS - atomic absorption spectrophotometry, ICPAES - inductively coupled plasma atomic emission spectrometry

**Table 4: Reference data of Zn concentration in normal prostatic fluid investigated by nondestructive XRF and EDXRF methods**

Reference	Method	n	Age, years M(Range)	Zn, mg/L M±SD
Birbaum et al 1961 <sup>[41]</sup>	XRF	-	-	490
Mackenzie et al 1962 <sup>[42]</sup>	XRF	8	37(25-55)	490±130
Zaichick et al 1981 <sup>[29]</sup>	EDXRF	15	-	580±183
Zaichick et al 1996 <sup>[30]</sup>	EDXRF	22	49(22-75)	590±210
Costello&Franklin 2009 <sup>[57]</sup>	EDXRF	24	-	588
Zaichick&Zaichick 2018 <sup>[58]</sup>	EDXRF	41	18-82	573±202
		13	28(18-40)	501±47
		38	59(41-82)	598±34
Zaichick&Zaichick 2018 <sup>[59]</sup>	EDXRF	42	31-75	559±204
Zaichick&Zaichick 2018 <sup>[60]</sup>	EDXRF	38	41-82	598±207
Zaichick&Zaichick 2018 <sup>[61]</sup>	EDXRF	38	41-82	598±207
Median of means, mg/L	580			
Range of means (M <sub>min</sub> - M <sub>max</sub> ), mg/L	490 - 598			
Ratio M <sub>max</sub> /M <sub>min</sub>	(598/490)=1.22			

M-arithmetic mean, SD – standard deviation of mean, XRF - X-ray fluorescence, EDXRF - energy dispersive X-ray fluorescence

There is some limitation in our study, which need to be taken into consideration when interpreting the results of this review. The sample size of each study was relatively small, and a total of 285 patients with prostatitis and about 900 normal controls were investigated from all 25 studies. As such, it is hard to make definitive conclusions about the clinical value of the Zn concentration in EPF as biomarker of prostatitis.

## Conclusions

The present study is a comprehensive study regarding the determination of Zn concentration in EPF as a biomarker for prostatitis. The study has demonstrated that Zn concentration levels are typically decreased in EPF samples of patients with prostatitis. The present study also demonstrates that EPF samples could be considered a reliable source for Zn biomarker analysis. Because of high heterogeneity, we recommend other primary studies.

## Ethics approval and consent to participate

Not applicable.

## List of abbreviations

CP, chronic prostatitis; TE, trace element; EPF, expressed prostatic fluid; AAS, atomic absorption spectrophotometry; ICPAES, inductively coupled plasma atomic emission spectrometry; XRF, X-ray fluorescence analysis; EDXRF, energy dispersive X-ray fluorescent microanalysis.

## Conflicts of Interest

None

## Authors' contributions

SZ analyzed and interpreted the data regarding the normal and inflamed prostate. VZ analyzed and interpreted the data regarding the analytical methods, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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