



Trace Elements in the Blood Serum and Their Possible Health Effects in Vellore District

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Abstract

It has long been believed that heavy metals possess many adverse health effects. Uncontrolled industrialization has released heavy metal pollution in the world. Heavy metal pollutants damage organ functions and disrupt physiological homeostasis. Diabetes mellitus is growing in prevalence worldwide. Several studies have indicated that the deficiency and efficiency of some essential trace metals may play a role in the islet function and development of diabetes mellitus. Some toxic metals have also been shown to be elevated in biological samples of diabetes mellitus patients. In the present work, we review the important roles of heavy metals in islet function and diabetes development in which the in vitro, in vivo or human evidences are associated with exposure to iron, copper, zinc, lead, chromium, magnesium and nickel. Through this work, we summarize the evidence which suggests that some heavy metals may play an important role in diabetes mellitus as environmental risk factors.

Keywords: Trace Elements, Blood Serum, Diabetes

1. Introduction

Heavy metals are among the most persistent of pollutants in the aquatic ecosystem because of their resistance to decomposition in natural conditions. High concentrations of these metals can be released into the aquatic environment as a result of leaching from bedrocks, atmospheric deposition, water drainage, runoff from riverbanks, and discharge of urban and industrial wastewaters.

The elemental anomaly in the groundwater regime once created through natural processes or

by unintended or unethical human intervention, often goes unabated. The toxicity of an element depends on the dose, the chemical form, route of exposure, bio-availability, distribution in the body, storage and excretion parameters.

In recent years, considerable interest has been focused on assessing the human health risk posed by metals, metalloids, and trace elements in the environment. It has long been recognized that large areas of the globe contain human populations characterized by having trace element

deficiency, or excess including chronic poisoning, Selinus and Frank, (2000); Bunnell, *et al.*, (2007).

Many current examples of environmental health problems are the result of long – term, low-level exposure to heavy metals. One notable example is the widespread poisoning caused by high arsenic levels in well waters in Bangladesh and West Bengal. During the past several decades, studies in a number of other locations have demonstrated widespread occurrence of trace elements in water at concentration significantly higher than the permissible limits, Soares *et al.*, (1999).

Elevated trace element concentrations are not limited to certain water types or polluted areas; they appear in all type of systems and in all geographic areas. It is clear that metal enters the aquatic system from diverse sources, both point and non – point and can be readily transported from abiotic to biotic system.

Places in Vellore District Tamilnadu, is famous for its leather industries. The population may be at risk because of mobilization of metals from the several chemical processes used by these industries. Most of these operations are conducted in dark alleys in the city where there is neither proper drainage nor a proper sewer system. It has been reported that at some places the effluents from the local industry has been pumped into the bore wells that joins the groundwater used for drinking purposes. To assess the mobilization of metals from these activities five Ground water samples were collected and analyzed for their trace element contents.

1.1. Health Status

In the third world countries environmentally related diseases are rampant. In the poor cities, environmental problems tend to originate in or around the home where crowding, smoky kitchen, garbage, pets, unsanitary food and dirty water continues to plague the inhabitants day in and day out. The inhabitants are susceptible to a range of environmentally related diseases owing to the high density of population. According to 2011 census, the population density of the study area is 3,936,331 with a sex-ratio of 1,007 females for

every 1,000 males, much above the national average of 929. Finkelman, (2007).

Vellore district is the main producer of leather in Tamilnadu; it has the major portion of the population engaged in leather related industries. A study related to health problems in Vellore District

Materials and Methods

2.1. Study Area

The study area lies between latitude 12°15' to 13°15' north latitudes and 78°20' to 78°50' east longitudes in Tamilnadu State. The total geographical area of the district is 6,077sq.km. (5,92,018hect). The district is bound on the northeast by Thiruvalluvar district, on the southeast by Kanjipuram district, on the south by Thiruvannamalai district, on the southwest by Krishnakri district, and on the northwest and north by Andhra Pradesh state. Major towns in the district include Ambur, Arakkonam, Arcot, Jolarpet, Pallikonda, Gudiyattam, Pernampbut, Melvisharam, Ranipet, Sholinhur, Tiruppattur, Vaniyambadi, Vellor and Walajapet.

Kaveripakkam is a panchayat twon in Vellore with the second largest lake in Tamil Nadu. The average maximum temperature experienced in the plains is 39.5 degree Celsius and the average minimum temperature experienced is 15.6 degree Celsius. The region experiences an average annual rainfall of 795 mm, out of which North East Monsoon contributes to 535 mm and the South West Monsoon contributed to 442 mm.

The Vellore District is one of the most vital and vibrant Districts in terms of industrial development in the State. The Vellore District has a dominant presence in the Leather and leather based industries. Vellore District accounts for more than 37% of the county's export leather and leather related products such as finished leather, shoe uppers, shoes, garments, gloves and so on. The Government of Tamilnadu provides all possible investment subsidies and infrastructural support in the form of setting up industrial estates and 9 common effluent treatment plants. Thus this

District share of the leather market in the years to come is ensured.

The District provides enough scope for the development and growth of industries engaged in Chemicals, Food processing, Sugar/Jaggery manufacturing, Synthetic Fibres, Fertilizers manufacturing, Textiles Garments, Steel castings and Auto bearing manufacturing. The existing units are facing two main problems viz., poor marketing and financial problems. Textile mills and rice mills, leather and leather based products belong more to the traditional category. Vellore visit is one of the recommended industrial tour, Other industrial attraction of Vellore are numerous medium and large scale industries like, BHEL, EID Parry, Tirumalai Chemicals and Greaves, SAME-DEUTZ, TVS-Brakes India, Mitsubishi, Greaves Cotton, MRF, Kramski Stamping and Molding India Pvt Ltd., RSL Industries Ltd, Farida Shoes Ltd etc.

2.2. Study subjects

The present study of diabetes mellitus (T2) and diagnosis was carried out in department of pathology, ESI hospitals in Vaniyambadi, Ambur, Pernambut, Vellore and Ranipet of Vellore district. The blood samples were taken from the tannery workers and tenants (outdoor patients as well as admitted patients), who have been advised by clinicians for blood sugar investigations. Workers have been advised for blood sugar investigations on the basis of symptoms and signs.

The study covered a sizable number of tannery workers (including office workers) in Vellore district (i.e.) 500 subjects which includes 284 males and 191 females and 25 of healthy controls (non-diabetes) of age between 25 - 65 years. These subjects are residing in several villages of five taluk of Vellore district (Vaniyambadi, Ambur, Pernambut, Vellore and Ranipet) and survey covered a distance of approximately 100 Km (on road). ESI Hospital admission survey has been carried out to collect the data with a standard questionnaire during the period of January 2012 to December 2014. Before enrolling the clinical study, all the patients were validated properly by

pre-clinical screening which includes signs a symptom of diabetes mellitus and laboratory investigation for diabetic screening and any complications of diabetes or other involvements such as cardiovascular, renal diseases. Standard methods are used for the various anthropometric measurements (blood grouping, blood glucose, blood cholesterol, TLC, D LC, urea creatinine, etc.,).

2.3. Data collection and classification

Around 500 datas were collected in the survey for the proposed work. The inputs designed for the system are age, gender, family background, period of working, taking medication for high blood pressure, found to have high blood glucose in a health examination during illness, smoking or using tobacco products, amount of vegetable and fruit intake, physical activity (30 minutes daily), body mass index, waist hip ratio, increased urination, hunger, thirst, poor wound healing, life style (labor class, sedentary work, retired persons and house wife's), gestational diabetes, frequent intake of non-vegetarian food, and itching all over the body.

2.4. Medical history

All of the recipient have no any other compliant apart from diabetic mellitus.

2.5. Sample Collection and Processing

About 10 mL of blood sample were collected from the ante-cubital vein of subjects using disposable needle and syringe. Samples were collected between 9.00-11.00 a.m. Each sample was taken in 5 mL plain specimen bottles and 5 mL fluoride-oxalate bottles after 12-14 hours overnight fast for analysis. The sample was centrifuged at 4000 rpm and the serum was separated and stored at -20 C until analysis.

2.6. Biochemical analysis

Determination of Cr, Pb, Fe, Cu, Mg, Mn, Zn and Ni levels in serum were measured by using Flame Atomic Absorption Spectrometer –Model Varian Spectra A240, (Sample volume – 10 mL per min. Burner – Air/Acetylene, N₂O/Acetylene

burner/ Gases hallow cathode – Acetylene and nitrous oxide) at Technology Business incubator Lab, Department of Science and Technology, VIT, Vellore, Tamilnadu.

2.7. Materials

All the chemicals under investigation are of analytical grade and were purchased from Nice Chemicals, Mumbai. During the analysis purified reagents were applied for preparation of solutions.

3. Results and Discussion

The results of the analysis are given in the **Table 1**.

3.1. Iron (Fe)

Iron is an essential transition metal required for the synthesis of two important functional proteins

Table-1: Trace elements concentration in the study area in mg/l.

S.No.	Workers Name	Cr	Pb	Fe	Cu	Zn	Mg	Mn	Ni
1	R.Kamal	0.588	0.662	8.377	0.705	2.286	7.307	0.325	0.726
2	N.Vetri	0.302	0.989	6.822	0.296	2.512	7.855	0.500	0.156
3	M.Vivek	0.987	0.926	7.783	0.629	2.351	6.891	0.615	0.287
4	T.Munisamy	0.993	0.124	8.834	0.328	2.412	6.342	0.650	0.388
5	A.Jakir	1.104	0.145	8.021	1.700	2.533	7.885	0.866	0.395
6	A.Rojamani	0.154	0.560	7.375	0.168	2.128	7.233	0.422	0.733
7	K.Rukku	0.142	0.876	5.720	0.319	2.114	6.788	0.650	0.188
8	T.Sangeetha	0.135	0.822	7.783	0.180	2.251	5.679	0.615	0.270
9	L.Padma	1.122	0.132	7.345	0.340	2.312	6.341	0.650	0.375
10	M.Vanitha	0.148	0.139	7.221	0.148	2.353	7.115	0.788	0.380

We observed that, the concentration of serum Fe level in tannery workers and healthy controls were found to range from 5.720 mg/L to 8.834mg/L and 0.0893mg/L respectively. Thus the elevated Fe level in serum oxidizes various biomolecules such as nucleic acids, proteins and lipids, which may contribute to diabetes 2 developments by decreasing insulin secretion from pancreatic beta cells with concomitant increase of insulin resistance, Worwood, (2002); Papanikolaou and Pantopoulos, (2005).

such as hemoglobin and myoglobin, which are involved in the transport of molecular oxygen during respiration. In blood stream small fraction of serum Fe is transported by a glycoprotein, called transferrin into the cells. In the body tissues, ferritin stores free Fe, which is increased in newly diagnosed diabetic subjects. A positive correlation between serum ferritin and Fe deposition in tissues, which linearly increased with diabetes duration, was already reported]. The serum ferritin elevation is regarded as an index of Fe overload, which successively leads to a condition called hemo chromatosis. Several studies showed association between hemo chromatosis and type 2 diabetes, Wiernsperger, Rapin, (2010); Acton *et al.*, (2006).

3.2. Magnesium (Mg)

Mg is the most abundant macro-nutrient which is essential for the maintenance of proper health. It is required for the activity of more than 300 enzymes, which serve several important physiological functions in the human body. Mg containing enzymes are involved in the glucose homeostasis, nerve transmission, DNA and RNA production. In prospective cohort studies an association was investigated between Mg consumption through diet and the risk of type 2 diabetes and was demonstrated that Mg deficiency might lead to a decrease in insulin mediated glucose uptake, Lopez-Ridaura *et al.*, (2004).

We observed that, the concentration of serum Mg level in tannery workers and healthy controls ranged from 5.679mg/l to 7.855mg/l and 0.1953mg/l respectively. Thus Mg supplementation prevented insulin resistance and also reduced the development of diabetes in animal models. Some studies reported low level of Mg in the blood serum and an increased urinary excretion of Mg in the diabetics relative to their healthy control subjects. Even though, higher Mg levels in serum may be a cause of diabetes in tannery workers, Swaminathan, (2003).

3.3. Manganese (Mn)

Manganese acts as a cofactor in several enzymes including those involved in bone marrow production and metabolism of carbohydrates, proteins and fats. It is essential for the proper utilization of choline, thiamine, biotin, vitamin C and vitamin E. Mn is also a cofactor of pyruvate carboxylase, which plays a role in the conversion of various non-carbohydrate compounds into glucose via gluconeogenesis for their subsequent use. Mn is also required for mitochondrial glycoproteins and normal insulin synthesis.

We observed that, the concentration of serum Mn level in male tannery workers ranged from 0.325mg/l to 0.866mg/l and that of healthy controls were 0.0022mg/l respectively the deficiency of Mn in serum may alter the metabolism and secretion of insulin, which has been implicated in diabetes development.

3.4. Copper (Cu)

Copper is an essential mineral, which is needed for several biological functions. Cu imbalance is implicated in cholesterol elevation by disrupting normal high density lipoproteins (HDL) and low density lipoproteins (LDL) balance. Cu also activates cytochrome oxidase which is involved in the electron transport chain of the mitochondria.

In case of copper deficiency, cytochrome oxidase reduces its activity which might lead to the distortion of mitochondria in metabolically active tissues such as pancreatic acinar cells, hepatocytes etc.

We observed that, concentration of Cu level in blood of tannery workers ranged from 0.180mg/l

to 1.700mg/l and that of the healthy control was 0.1489 mg/l respectively.

The increase in the concentration of serum Cu levels in tannery workers with diabetic may attribute to hyperglycemia that may stimulate glycation and release of copper ions from copper-containing enzymes. These observations are supported by the findings that copper have antioxidant activity because not only Cu constitute the active sites and stabilize the conformation of several antioxidant enzymes, but it also compete for copper- binding sites and can provide protection against transition metal-mediated and free radical-induced injury. The relationship between an increase in Cu concentration and the oxidation of low-density lipoproteins has been confirmed, and has been linked to disorders in the structure of the arterial walls, stress, infection, and diabetes mellitus.

2.6. Zinc (Zn)

Zinc is an essential trace element which is required for normal cell processing e.g. cell division and apoptosis. More than 300 enzymes need Zn for their catalytic activities. About 70% of the Zn is bound to albumin and any pathological alteration of albumin affects the serum. Zn plays a key role in the storage and secretion of insulin, which subsequently increases the uptake of glucose. The Zn transporter (ZnT8) is a key protein for the regulation of insulin secretion from the pancreatic β -cells is already studied.

The decrease in Zn may potentiate the toxicity of other metals such as iron and copper. Zinc deficiencies in diabetics are associated with excess free-radical activity and the increased oxidation of lipids, damaging the heart, arteries and other integral parts of the vascular system.

We observed that, concentration of Zn level in blood of tannery workers ranged from 2.114mg/l to 2.533mg/l and that of the healthy control was 3.247 mg/l respectively. The studies revealed that type 2 diabetic workers have low level of Zn in blood due to its increased urinary depletion. As a result, hypozincemia and hyperzincuria are developed in diabetics.

2.7. Chromium (Cr)

Trivalent form of Cr has high biological activity which is required for the optimal glucose uptake by cells. Cr regulates insulin and blood glucose levels by stimulating insulin signaling pathway and metabolism by up-regulating glucose transporter (GLUT4) translocation in muscle cells. Cr deficiency results in the elevation of blood glucose levels and if it is persisted for a prolonged period, it may lead to the development of diabetes, Qiao *et al.*, (2009).

We observed that, concentration of Cr level in blood of tannery workers ranged from 0.135mg/l to 1.122mg/l and that of the healthy control was 0.0292mg/l respectively.

Some reports showed that Cr supplements decrease the blood sugar level in diabetes. Prolonged hyperglycemia increases Cr urinary excretion. Generally Cr maintains the normal human physiology while its imbalance predisposes to glucose intolerance which subsequently converts to diabetes related complications.

The concentration of Cr level in the urine of controls were lower than those of workers, but the difference was not significant ($p > 0.05$). These results are in good agreement with other investigations. For example, Anderson elucidated the action of Cr in diabetes and showed that the administration of Cr may have beneficial effects on this disease. Others have demonstrated that severe Cr deficiency led to fasting - hyperglycemia, glycosuria, and impaired growth. In general, in addition to impaired Cr utilization, age plays a major role in the status of Cr. Results from some trial studies have shown that Cr supplementation increases muscle gain and fat loss associated with exercise and improves glucose metabolism and the serum-lipid profile in workers with or without diabetes. Chromium is involved in both carbohydrate and lipid metabolism. Insufficient dietary Cr is associated with increased risk factors linked with non-insulin dependent diabetes and cardiovascular diseases. Most of the tannery workers understudied have cardiac problems, and they are also consistent

with other studies, which reported that Cr deficiency has also been held responsible for vascular complications associated with diabetes mellitus, Anderson, (1998); Cefalu, *et al.*, (2002).

2.8. Lead (Pb)

Lead is hazardous to most of the human body organs, and interferes with metabolism and cellular functions. Several studies demonstrated that environmental exposure to Pb badly affects the antioxidant pathways. Lead induced toxicity may cause derangement of antioxidant mechanisms in living tissues; as a consequence highly reactive oxygen species (ROS) are generated. This antioxidant imbalance might lead to the degradation of proteins, nucleic acids and lipid peroxidation. An oxidative attack of cellular components by ROS is implicated in the pathogenesis of diabetes, Yabe, *et al.*, (2011).

We observed that, concentration of Pb level in blood of tannery workers ranged from 0.124mg/l to 0.989mg/l and that of the healthy control was 0.0125mg/l respectively. The higher concentration of Pb in the biological samples (i.e. blood plasma) of diabetics than the non-diabetics was already reported.

2.9. Nickel (Ni)

The toxic metal of Ni may have a role to induce renal tubular dysfunction in diabetic subjects. Subsequently dysfunctional kidneys may become a potential source for the loss of several essential trace elements through urine voiding rather than their retention in blood plasma serum in order to retain the homeostasis of blood and other tissues were already reported, Kubrak *et al.*, (2012).

We observed that, concentration of Ni level in blood of tannery workers ranged from 0.156mg/l to 0.733mg/l and that of the healthy control was 0.0012mg/l respectively.

The tannery workers have high level Ni in serum and it has been observed that kidney is the major organ for Ni accumulation, thus contributes in renal dysfunction, Yarat *et al.*, (1992).

Recent studies in rats and humans indicate that nickel deprivation depresses growth, reproductive performance, and plasma glucose and that it alters the distribution of other elements in the body including calcium, iron, and zinc. Bonnefont-Rousselot investigated the use of vanadium, chromium, magnesium, zinc, and selenium as well as α -tocopherol, ascorbic acid, nicotinamide, and riboflavin supplements in diabetic patients, with a particular focus on the prevention of complications originated by the disease. It was also reported that dietary supplementation with micronutrients may be a complement to classical therapies for preventing and treating diabetic complications and the supplementation is expected to be more effective when there is a deficiency of these micronutrients, Nielson, (2000).

4. Conclusion

It can be concluded that impaired trace-element metabolism may have a role in the pathogenesis and progression of type-2 diabetes mellitus. The increases of Fe, Cr, Pb, Cu and Mg together with decreases of Zn, Mn and Ni concentrations in serum of tannery workers may be involved in disturbances of insulin secretion or its action as compared to the healthy subjects. The high levels of Cu and Fe in tannery workers of both age groups and genders disrupt the antioxidant functions and enhance the lipid peroxidation. Oxidative modification of lipoproteins, particularly low-density lipoprotein, may be at least one cause of vascular complications of diabetes. The low level of zinc seen in the workers is possibly due to increased urinary excretion of this essential trace element .

The tannery workers are diagnosed with diabetes and are found to be Type II diabetes which is used

to be exclusively found among older workers and some of them are young adult workers due to obesity. Type II diabetes occurs when the pancreas still makes insulin, but the body develops resistance to insulin, so the fat cells don't absorb insulin as well as muscle cell do. They are unable to take up the sugar that is in the blood. Several reports showed that the pancreas has to work harder to pump increased levels of insulin

into the blood to compensate for resistance, that the pancreas eventually wears itself out and can no longer keep up with the demand. Oral medications, combined with a low fat, high fibre diet and exercise is usually enough to control the symptoms of type 2 diabetes.

To prevent diabetes related morbidity and mortality, there is an immense need of dedicated self-care behaviors in multiple domains, including food choices (low fat and high fiber diet), physical activity (exercise), proper medications intake and blood glucose monitoring from the tannery workers who have diabetes. Though multiple demographic, socio-economic and social support factors can be considered as positive contributors in facilitating self-care activities in diabetic patients, role of clinicians in promoting self-care is vital and has to be emphasized. Realizing the multi-faceted nature of the problem, a systematic, multipronged and an integrated approach is required for promoting self-care practices among tannery workers having diabetes to avert any long-term complications.

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