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Research Article

ALTERATIONS IN ANTI-MICROBIAL PROTEINS AND PRO-INFLAMMATORY CYTOKINES IN FEMALES OF ELDER AGE SUFFERING FROM IRON DEFICIENCY ANEMIA

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Abstract:

Objective: Iron Deficiency Anemia is very common issue of nutrition especially among females and it is also common in elder ages. Aging enhances the inflammatory mediator's levels in plasma such as acute phase protein and pro-inflammatory cytokines. There is little information available about the alteration in the anti-microbial proteins in the females of elder age with iron deficiency anemia. In this current research work, we aimed to find out the alterations in the pro-inflammatory cytokines and recently identified anti-microbial proteins like defensin, hepcidin and chemerin in females of elder age suffering from iron deficiency anemia.

Methodology: In this research work, we used the samples of blood of 20 healthy females (55.0±7.0 years of average age) and 20 females suffering from Iron Deficiency Anemia (58.0±6.0 of average age). This research work was carried out in DHQ Hospital Rajanpur from November 2018 to August 2020.

Results: In this current research work, levels of CRP (C - Reactive Protein) ($P<0.010$), TNF- α (Tumor Necrosis Factor- α) ($P<0.050$) and IL-6 (Interleukin-6) ($P<0.050$) were much high in the group of Iron Deficiency Anemia when we compared them with the members of healthy group. The levels of hepcidin ($P<0.0010$), chemerin ($P<0.050$) and defensin levels ($P<0.050$) were also much high in the patients as compared to the healthy groups.

Conclusion: We discovered that there is occurrence of inflammatory changes in the females of elder age suffering from iron deficiency anemia. Besides the levels of pro-inflammatory cytokine (CRP, IL-6 and TNF- α), the levels of anti-microbial proteins (hepcidin, chemerin and defensin) were also much higher in the females of elder age suffering from Iron Deficiency Anemia because of the presence of different inflammatory alterations.

Keywords: Anti-Microbial, Anemia, Tumor Necrosis Factor-A, C - Reactive Protein, Cytokines, Iron Deficiency, Inflammatory.

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INTRODUCTION:

One of the inevitable process is aging that is much affected by the environment, genetic and lifestyle. There is still no fully understanding of the underlying mechanisms of this process of aging. It is also discovered that there is close association of the aging with an increase in pro-inflammatory cytokines [1]. One of the important micronutrients is iron that plays a much vital role in our body. The requirement of the daily dietary iron is about one mg for males and 2 to 3 mg for females and adolescences. The iron intake is approximately 15.0 mg daily with the diet and only 5.0% to 10.0% of this proportion is absorbed in the bowel. Iron Deficiency Anemia is resulted by the issues in hemoglobin's synthesis. Iron Deficiency Anemia diagnosis is that the level of hemoglobin of lower than 11.50 g/dl in females and lower than 13.50 g/dl in males. This case similar in the whole world. Aging is an important risk factor for developing the Iron Deficiency Anemia due to the intake of drugs, improper absorption in bowel and appetite changes [2]. Cytokines perform a very important role in the regulating the inflammatory response. The cause behind the increased prevalence of anemia in elder age may be dis-regulation of the pro-inflammatory cytokines (as CRP, TNF- α and IL-6) with the increase of age. Increased levels of pro-inflammatory cytokines directly or indirectly restrict the erythropoietin and thus may result in anemia [3].

AMPs (Anti-microbial Peptides) and proteins perform much vital role in the defense of human immunity. AMPs are very important elements in innate immunity and they can possess the functions like apoptosis and healing of wound. Come of anti-microbial proteins are defensin, hepcidin & chemerin [4]. When there is adequate iron store, there is an increase in the production of the hepcidin in liver. During the anemia, hepcidin forms a vital link between the defense of the body, iron metabolism and inflammation. One research work conducted in the past stated that during inflammation and infection, there is considerably increase in the synthesis of the hepcidin stimulated by IL-6 [5]. Chemerin play its role in the migration of the immune cell, adipo-genesis, and glucose homeostasis and osteoblast-genesis. It is much abundant in the epidermis of the human being to ensure the barrier [6]. Lehrke in 2009 stated that there is strong association of the chemerin with the parameters of inflammation [7]. Defensin contribute to the host defense in internal site of small intestine and skin [8]. There are three groups of defensin as θ -defensins, α -defensins and β -defensins. But in human beings, only α -defensin and β -defensins are present [9, 10]. Decreased expression of the defensins

compromises the immunity of host and thus may alter the balance towards the inflammation [11]. Although immune changes in the complication of anemia has been subjected of various investigations [12]. But still there is less information available about the alterations in anti-microbial proteins in females of elder age suffering from iron deficiency anemia. The rationale of this research work was to find out the alterations in the pro-inflammatory cytokines and newly identified anti-microbial proteins in elderly females with iron deficiency anemia.

METHODOLOGY:

We took the samples of blood from 20 healthy females (average age of 55.0 ± 7.0 years) and 20 females suffering from Iron Deficiency Anemia (average age of 58.0 ± 6.0 years). This research work was carried out at DHQ Hospital Rajanpur from November 2018 to August 2020. Females suffering from other inflammatory complications, females with diagnosed chronic complications and females who were using antibiotics from last four weeks were not included in this research work. Ethical committee of the institute gave the permission to conduct this research work. The group of the patients suffering from Iron Deficiency Anemia was comprised of females who were present with level of hemoglobin < 11.50 g/dL, plasma iron of < 30.0 mg/dL and level of ferritin < 15.0 ng/mL. We obtained the 3mL venous blood from all the females and places the samples in anti-coagulant tubes. We separated the plasma from the samples for performing the biochemical analysis. We placed the samples of plasma in the Eppendorf tubes and stored all the plasma samples at -80.0°C , until the time of analysis.

We used an automatic analyzer for the diagnosis of the level of plasma ferritin, iron and hemoglobin with the utilization of the commercial kit provided by the manufacturer. The methods for the determination of the levels of hormones were carried out as recommended in applicable catalogues, utilizing the microplate reader. We used the ELISA kit for the measurement of the plasma levels of chemerin, TNF- α , IL-6, defensin, hepcidin and CRP. We used the SPSS V. 20 for the statistical analysis of the data gathered in this research work. We expressed the data in averages with standard deviations. The data of the normality tests was subjected for statistical differences between the participants of both groups with the utilization of ANOVA.

RESULTS:

In this current research work, levels of CRP ($P < 0.010$), TNF- α ($P < 0.050$) and IL-6 ($P < 0.050$) were much high in the patients suffering from Iron Deficiency Anemia

as compared to the members of healthy group. The levels of plasma hepcidin ($P<0.0010$), chemerin ($P<0.050$) and defensin ($P<0.050$) were identified as

much high in the group of patients as compared to the groups of healthy controls (Table-1).

Table-I: Changes in Pro-Inflammatory Cytokines and Antimicrobial Proteins Profile Between the Control Group and Group With IDA

Parameters	Healthy Controls n=20	Group with IDA n=20
CRP (mg/L)	1.5±0.6a	3.4±1.5b
TNF- α (pg/mL)	36.45± 12.4a	58.21±17.9b
IL-6 (pg/mL)	20.72±10.6a	39.55±12.1b
Defensin (ng/mL)	10.5±2.6a	21.2±3.5b
Hepcidin (ng/mL)	165.5±50.8a	246.70±46.1b
Chemerin	89.5±25.4a	111.5±31.8b

a, b signs indicate statistical differences among the groups ($p<0.05$).

DISCUSSION:

Aging is inevitable process and it is much affected by the lifestyle, genetic and environmental features. There is still not fully understanding of the aging process. There is association of aging with the inflammation and biomarkers like IL-6 [13]. The process of aging might be an important risk factor in progress and developing of Iron Deficiency Anemia with the dysregulation of some pro-inflammatory cytokines. These research works about the alterations of the anti-microbial proteins throughout the process of aging and in deficiency of iron are not much sufficient. In this research work, we stated that anti-microbial proteins like defensin, hepcidin, and chemerin, pro-inflammatory cytokines like IL-6 and TNF- α and acute phase proteins like CRP increases in the females present with elder age suffering from iron deficiency anemia. Penninx in year 2004 have discovered that persons suffering from anemia have significantly high levels of IL-6, CRP, and TNF- α [14]. Gonzalo-calvo in 2010 stated that TNF- α is the main aging indicator and there is increase in its levels in the elder population [15].

Roubenoff in 1998 also stated that IL-6 production was much high in the elder population as compared to the young persons. There is correlation of the increased IL-6 with the increased CRP, which is an inflammation marker [16]. Inflammation is main cause of stimulation of the hepcidin synthesis. There is an increase in inflammation with the increase of age, therefore, the levels of hepcidin also rises. There is capability of the β -defensin to inhibit the inflammation. TNF- α induces the expression of the defensin in keratinocytes but this mechanism is not clear [10]. Lehrke in 2009 stated that there is strong

association of the chemerin with the parameters of inflammation. We correlated the chemerin levels with the concentrations of the IL-6, CRP and TNF- α . TNF- α induces the synthesis of chemerin. There are some research works that stated that the levels of chemerin can increase with the increase in age [8]. Zylla in 2017 have concluded the levels of chemerin are much high in females as compared to the males. In this current research work, the levels of chemerin in the patients of Iron Deficiency Anemia were very high as compared to the females of control group.

CONCLUSIONS:

The results of this research work concluded that there is occurrence of the inflammatory alterations in the females of elder age suffering from iron deficiency anemia. Besides the levels of pro-inflammatory cytokine (CRP, IL-6 and TNF- α), the levels of anti-microbial protein (hepcidin, chemerin and defensin) were discovered as much high in the elderly females suffering from iron deficiency anemia due to inflammatory alterations.

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