International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2024; 7(2): 07-11
Received: 10-05-2024
Accepted: 14-06-2024

Amal El Sayed Farag
Dermatology and Venereology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Shady Fikry Abdelsalam
Dermatology and Venereology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Yasmina Ahmed EL Attar
Dermatology and Venereology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Rowida Raafat Ibrahim
Biochemistry Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Yomna Mazid El Hamd Neinaa
Dermatology and Venereology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author:
Amal El Sayed Farag
Dermatology and Venereology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Cysteine and Glutamine level in hair shaft fractures patients

Amal El Sayed Farag, Shady Fikry Abdelsalam, Yasmina Ahmed EL Attar, Rowida Raafat Ibrahim and Yomna Mazid El Hamd Neinaa

DOI: https://doi.org/10.33545/26649411.2024.v7.i2a.185

Abstract
Hair shaft problems induced by extrinsic factors include environmental factors such as physical trauma like UV radiation or cosmetic treatments as thermal damage caused by hair dryers, ironing, and hair curling devices. Also, chemical straightening and hair coloring are examples of chemical causes of hair shaft fracture. Hair shaft fractures have a wide range of types and forms. These structural defects are linked to hair fragility and can be hereditary or acquired. Trichorrhexis nodosa, monilethrix, pseudo monilethrix, pili torti, trichoschisis, trichorrhexis invaginata and pseudopili annulati are all examples of hair shaft disorders. Cysteine, a semi-essential amino acid that is abundant in hair, plays a crucial role in maintaining the stability of the hair shaft through its involvement in disulfide bond formation. Glutamine might be a substantial source of energy for tissues that use aerobic glycolysis. As a result, metabolic data indicates that glutamine is a substantial fuel source in the hair follicle.

Keywords: Cysteine and Glutamine, hair follicle, shaft fractures patients, cortex and medulla

Introduction
The hair shaft is a three-layered keratinized circular cylinder of thick layer of packed spindle-shaped cortical cells and a center fragile medullar layer that is not always present. The basic structure of hair shaft is cuticle, cortex and medulla [1].
Any genetic or environmental abnormalities in this typical structure might result in changes in its physical characteristics such as shape and strength. When a patient's hair texture, appearance, or capacity to grow hair long changes, hair shaft fracture is suspected. Patients commonly complain from lack of apparent hair growth, hair breaks easily at tips (fragile hair), split ends and whitish discoloration with multiple small white spots at hair tips or along length of hair shaft [2].
Cysteine is a non-essential amino acid that has a role in protein synthesis, making collagen and other metabolic processes [3]. Glutamine is involved in a variety of metabolic events within cells and plays a key role in tissue-specific and inter-tissue physiological activities.

Embryology of the hair
The hair follicle is one of our body's most complicated organs with a complex structure and a variety of activities. Hair follicle growth occurs mostly during prenatal and neonatal skin development. It includes coordinated ectodermal-mesodermal interactions [4]. All epithelial components of the hair follicle are produced by ectodermal hair follicle stem cells. Whereas mesoderm-derived cells give birth to the follicular dermal papilla and the connective tissue sheath. Instead, neural crest-derived melanocyte gives birth to the pigmentary unit of the hair follicle [5].

Hair shaft structure
The hair shaft's cuticle is a sulfur-rich material. Each cuticle scale is made of multiple layers (epi-, exo-, and endocuticle) and contains varying amounts of sulphur. The cuticle can be one or several layers thick. Cuticular scale shape is influenced by biomechanical patterns of cell deformation during hair follicle differentiation [6].
The cortical layer is made up of tightly fitting spindle-shaped keratinized cells that are sulfur-rich. It has a filamentous structure that causes hair to break along the long axis [7].

It is heterogeneous and "bilaterally asymmetric," and may be separated into ortho and par cortex based on the pattern of micro fibrils and their arrangement on the shaft [8]. It consists primarily of intermediate filaments (IFs) and keratin-associated proteins (KAPs) [9].

There are many morphological characteristics of the cuticle. An annular cuticle is the one in which one scale covers the whole shaft (coronal). A nonannular cuticle, on the other hand, is a cuticle with many scales that fit across the shaft. There are two another opposit types: Noninverted (the free scale margin is directed upstream the shaft) and, less frequently, inverted (the free scale margin is directed downstream the shaft) [10]. (Figure 1).

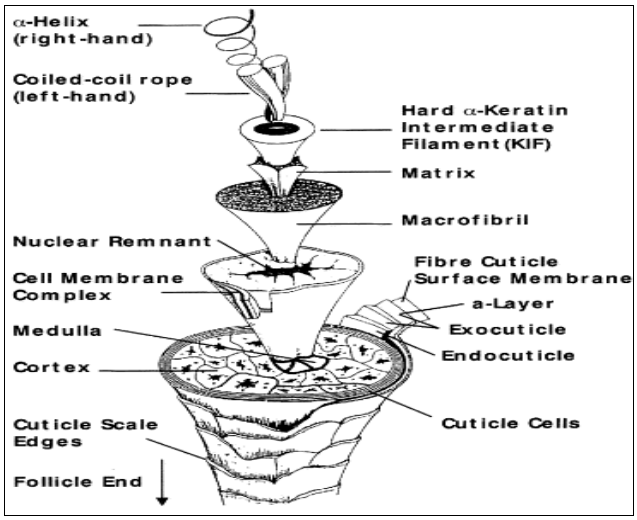

Fig 1: Hair shaft structure [11]

Causes of hair shaft fractures:

Hair shaft disorders can be classified into hair shaft disorders without increased fragility that is mostly congenital as pili annulati, pseudo pili annulati, woolly hair and Uncalmable hair syndrome and hair shaft disorders with increased fragility that could be congenital as congenital trichorrhexis nodosa (arginosuccinic aciduria), Monilethrix, Pili torti, Trichorrhexis invaginata, Trichothiodystrophy, or Acquired as acquired trichorrhexis nodosa and Bubble hair [12].

Hair shaft damage can result from [13]

- External exposure to thermal causes such as high amounts of heat used in flat irons, curling irons, and blow dryers. Brushing, rubbing, tugging, and pulling on damp hair causes mechanical damage to the connections.
- Physical causes like sun damage, humidity extreme weather conditioners, pollution, and other factors can have an adverse effect on the hair's bonds.
- Damage can also be caused by chemical services such as color, lighteners, relaxers and keratin treatments.
- Chemicals and/or thermal tools react with disulfide bonds, breaking them and triggering protein loss, leaving damaged hair behind as a result of damage to the disulfide bonds throughout the hair fiber.

When a disulfide bond breaks, there are two types of responses that might occur:

The solitary sulphur hydrogen component pairs with a single oxygen molecule in the first reaction. This completes the pair, preventing any further harm. Hair damage happens in the second response, a sulphate group ($S0_3$), is formed when a single sulphur hydrogen molecule combines with three oxygen molecules. Cystic acid is the name for protonated sulphate. The protein in the hair is then eaten away by cystic acid [14].

Amino acid composition in hair shaft

Hair is mostly made up of keratin protein (65-95%), with water, lipids, and trace elements making up the rest. Keratin can be presented as one of two forms; the first form is alpha keratin, the most important component of human scalp hair, contains all the 21 amino acids in varying amounts. The second form is beta-keratin, the major protein found in nails, skin, and hair [15]. A variety of variables, including age, sex, hair color, race, as well as dietary habits and geographic origin, are known to influence the amino acid content of hair [16]. For example, coinciding with increasing age, there is a significant increasing in serine, arginine, and proline concentrations, with concomitant decrease in aspartic acid, glycine, alanine, valine, isoleucine, lysine and cysteine in concentrations were reported. Also, dietary habits may have a role in the identification of essential amino acids in human hair, non-essential amino acids are more likely to be affected by genetic or phenotypic variables [17].

Cysteine

Cysteine is a non-essential amino acid that has a role in protein synthesis, making collagen and other metabolic processes. It's found in beta-keratin. It affects skin elasticity and texture. In rare cases, cysteine may be essential for infants, the elderly, and individuals with certain metabolic diseases or who suffer from malabsorption syndromes. Cysteine can usually be synthesized by the human body under normal physiological conditions if a sufficient quantity of methionine is available [3].

Dietary sources [18]

Cysteine may be obtained from both animal and plant sources. There are many cysteines rich foods like soya foods, Poultry, Red Pepper, Garlic, cheese, grains, yogurt, broccoli, egg fish, milk, onion, oats, dates and sunflower seeds [18].

- Soy Foods: Unsalted and roasted soybeans are low in cholesterol and high in cysteine.
- Turkey, chicken, and other bird meals are rich providers of cysteine, a protein that the body requires.
- Red pepper has a lower amount of cysteine than dairy and poultry products. The quantity of cysteine present in garlic is nearly the same as that found in red pepper.
- Cheese is high in cysteine since it is a dairy product.
- Grains are high in cysteine.
- Greek yoghurt is claimed to have the most Cysteine, as well as other vital amino acids such as Lysine. Milk is one of the greatest Cysteine-containing foods, because of its high calcium content. It is thought to be the finest source of Cysteine.
- Broccoli is regarded as one of the most nutrient-dense vegetables for a reason that is high in cysteine.
- Eggs are high in cysteine. In addition to cysteine, eggs include vitamins B and D, and selenium.
- Fish is one of the most significant Cysteine meals. Fish are high in Methionine, which is required for the body's

generation of Cysteine. This increases the natural production of cysteine in an indirect way.
- Onions are another source of Cysteine. Onion is also a good source of Methionine, which the body uses to make Cysteine.
- Oatmeal is one of the healthiest foods on the market. Cysteine, Methionine, Threonine, Isoleucine, and Tyrosine are among the essential and non-essential amino acids found in them. Another plant-based source of Cysteine is dates. They're high in cysteine and a variety of other amino acids.
- Sunflower seeds are another high-protein food that is high in Cysteine. The health advantages of these seeds are numerous. They're recognized for their healthy fatty acids, which can help the body decrease harmful cholesterol levels.

Now that the importance of cysteine in the body has been established, it's time to incorporate these cysteine-rich foods into everyday diet. Artificial supplements are frequently provided to people who have been diagnosed with Cysteine deficiency. With such high levels of Cysteine in these meals, man may confidently use them to address his issues [18].

Cysteine biochemistry

Cysteine is a naturally occurring sulphur-containing amino acid that is found in most proteins. It has a Sulfhydryl group (thiol group) which acts as a functional group that composed of a sulphur atom and a hydrogen atom (-SH). It is responsible for a variety of vital cysteine activities, including permitting the creation of disulfide bonds, which are essential for determining the structures of many proteins [19].

Also, thiol groups may play an important role in metal binding, enzyme catalysis and oxidation/reduction processes. The reactive thiol side chain that plays these tasks can also have a detrimental influence on a protein's function by forming improper disulfide bonds or other harmful changes. Cysteine thiols' high reactivity and sensitivity to damage by reactive oxygen species put cysteine-containing proteins under oxidative selection pressure [20]. (Figure 2).

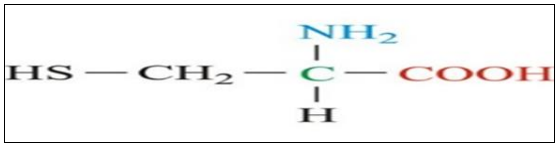

Fig 2: Cysteine structure [21]

Cysteine showing disulfide bond:

Cysteine oxidation can result in the formation of a disulfide bridge, which is a single covalent link formed by the coupling of thiol groups [22]. Many proteins rely on cysteine's disulfide bonds to define their final tertiary and quaternary configuration by stabilizing the folded structure. Hence, disulfide bridges generated between cysteine residues in peptides and proteins are important molecular architectural building elements that can regulate basic biological processes [23].

A two-electron oxidation pathway leads from reduced sulfhydryl groups of cysteines (S-H) to the oxidized cysteine (S-S) residue when two side chain S atoms of spatially proximal cysteines form a disulfide bond [24].

This process is frequently facilitated and accelerated in cellular contexts by enzymes such as protein disulfide isomerizes. Disulfide bridges are the sole natural covalent bond between polypeptide strands and can be created intermolecular even between two vicinal cysteines. They may also exist as an intermolecular characteristic, resulting in enhanced protein aggregation. The cleavage of disulfide bonds in biomolecules can cause the native conformation and biological function to collapse. As a result, defects in the creation of disulfide bonds can cause serious problems, such as the buildup of protein aggregates, cellular stress, and cell death [25].

Cysteine as Antioxidant

Cysteine is one of the body's most powerful antioxidants and destroyers of harmful waste products that are thought to hasten the ageing process. It has antioxidant effects due to its capacity to conduct redox reactions. It is a necessary precursor for the creation of the antioxidant glutathione, which protects cells in the human body from free radicals [26].

Cysteine Role in Hair

The presence of amino acids-especially cysteine in cuticles help to keep moisture in the hair. Hair that is dull and dry is an indication of significant cuticle damage and an amino acid deficiency. Cysteine has a key function in hair strength, and blends reinforced with Cysteine can assist to strengthen hair. This amino acid promotes healthy hair development, strengthens hair, and allows it to endure everyday style and manipulation [27, 28].

Glutamine

Glutamine is a non-essential amino acid with distinct metabolic activities. It is the most prevalent free amino acid in circulation and intracellular pools, it accounts for more than 60% of the free amino acid pool in skeletal muscle, which includes nearly half of the total free amino acids in the body [29]. (Figure 3).

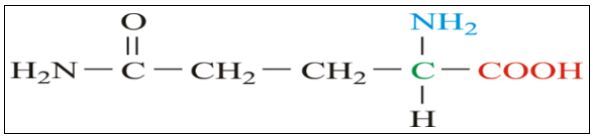

Fig 3: Glutamine structure [30]

Also, it is a precursor to produce amino acids, proteins, nucleotides, and a variety of other physiologically significant compounds [31].

Metabolic role of Glutamine

Glutamine is involved in a variety of metabolic events within cells and plays a key role in tissue-specific and inter-tissue physiological activities.

Glutamine is a key transporter for the movement of nitrogen and carbon across body tissues, as well as a precursor and nitrogen donor for several biosynthetic pathways including ammonia-genesis [32]. It has regulatory effects in skeletal muscle, including the promotion of protein synthesis and the prevention of protein breakdown. It has been demonstrated to promote glycogen production in the liver through an unidentified mechanism [33].

Glutamine role in hair

It's been proposed that glutamine might be a substantial source of energy for tissues that use aerobic glycolysis. As a result, metabolic data indicates that glutamine is a substantial fuel source in the hair follicle [34].

In humans, glutamine is one of the major amino acids that leads to consistent hair development. Despite the fact that it is created naturally by the body, it decreases with age. Hair loss can be caused by a lack of a few necessary and non-essential amino acids [35].

Glutamine may be found in a variety of foods like eggs, beef, milk, white rice and corn. Glutamine supplements may aid digestive, immunological, and other systems, particularly during times of stress when the body consumes more energy [36].

Conclusion

The hair shaft is a complex, multi-layered structure consisting of the cuticle, cortex, and medulla, each contributing to the overall integrity and function of hair. Disruptions in these layers, whether due to genetic or environmental factors, can significantly affect hair's physical properties such as strength and elasticity, leading to conditions like hair shaft fractures. Essential amino acids like cysteine and glutamine play crucial roles in maintaining hair health. Cysteine, vital for keratin synthesis, enhances hair strength and elasticity, while glutamine serves as a significant metabolic fuel, supporting consistent hair growth. Incorporating these amino acids into the diet can aid in maintaining healthy hair.

Conflict of Interest: Not available

Financial Support: Not available

References

1. Huang WY, Lin ET, Hsu YC, Lin SJ. Anagen hair follicle repair: Timely regenerative attempts from plastic extra-bulge epithelial cells. Exp Dermatol. 2019;28:406-12.
2. Villani A, Ferrillo M, Fabbrocini G, Garza OSS, Scalvenzi M, Ruggiero A. Hair aging and hair disorders in elderly patients. Int J Trichology. 2022;14:191-6.
3. Cruz CF, Azoia NG, Matamá T, Cavaco-Paulo A. Peptide-protein interactions within human hair keratins. Int J Biol Macromol. 2017;101:805-14.
4. Groot DSC, Ulrich MMW, Gho CG, Huisman MA. Back to the future: From appendage development toward future human hair follicle neogenesis. Front Cell Dev Biol. 2021;9:661787.
5. Chermnykh E, Kalabusheva E, Vorotelyak E. Extracellular matrix as a regulator of epidermal stem cell fate. Int J Mol Sci. 2018;19:1003.
6. Breakspear S, Noecker B, Popescu C. Mechanical anisotropy of hair affected by genetic diseases highlights structural information related to differential crosslinking in keratins. Eur Biophys J. 2023;52:53-67.
7. Harland DP, Plowman JE. Development of hair fibres. Adv Exp Med Biol. 2018;1054:109-54.
8. Vsevolodov EB, Mussayeva AS, Latypov IF, Burlakova OV, Nikeryasova EN, Golichenkov VA. Some paradoxical phenomena in hair follicle histophysiology. Russian Journal of Developmental Biology. 2021;52:9-15.
9. Baltenneck F, Genty G, Samra EB, Richena M, Harland DP, Clerens S, *et al*. Age-associated thin hair displays molecular, structural and mechanical characteristic changes. J Struct Biol. 2022;214:107908.
10. Harland DP, Novotna V, Richena M, Velamoor S, Bostina M, McKinnon AJ. Helical twist direction in the macrofibrils of keratin fibres is left handed. J Struct Biol. 2019;206:345-8.
11. Wortmann FJ, Wortmann G, Sripho T. Why is hair curly?-Deductions from the structure and the biomechanics of the mature hair shaft. Exp Dermatol. 2020;29:366-72.
12. Ahmed A, Almohanna H, Griggs J, Tosti A. Genetic hair disorders: A review. Dermatol Ther (Heidelb). 2019;9:421-48.
13. Reda EM, Ghazal H, Othman H, Hassabo AG. An observation on the wet processes of natural fabrics. Journal of Textiles, Coloration and Polymer Science. 2022;19:71-97.
14. Lyakhovitsky A, Kartvelishvily E, Drousiotis T, Lyakhovitsky K, Baum S, Barzilai A. Hair shaft morphology, elemental composition, and nanoparticles in frontal fibrosing alopecia: A case-control study. Acta Derm Venereol; c2021, 101.
15. Yenmiş M, Ayaz D. The story of the finest armor: Developmental aspects of reptile skin. J Dev Biol; c2023, 11.
16. Rudnicka L, Olszewska M, Waśkiel A, Rakowska A. Trichoscopy in hair shaft disorders. Dermatol Clin. 2018;36:421-30.
17. Zhang L, Liu J, Sui SY, Dong CH, Xu JT, Zhu P. Study on the preparation and characterization of cross-linked film of human hair keratin and cellulose. Ferroelectrics. 2017;521:77-85.
18. Alqhazo M, Rashaid AB. Amino acids profiles of children who stutter compared to their fluent sibling. Int J Psychiatry Clin Pract. 2020;24:301-8.
19. Rashaid AB, Khasawneh Z, Alqhazo M, Nusair S, El-Khateeb M, Bashtawi M. Underivatized amino acid analyses using liquid chromatography-tandem mass spectrometry in scalp hair of children with autism spectrum disorder. International Journal of Chemical and Molecular Engineering. 2021;15:59-64.
20. Margaritelis NV, Chatzinikolaou PN, Bousiou FV, Malliou VJ, Papadopoulou SK, Potsaki P, *et al*. Dietary cysteine intake is associated with blood glutathione levels and isometric strength. Int J Sports Med. 2021;42:441-7.
21. Cardoso FC, Lewis RJ. Structure-function and therapeutic potential of spider venom-derived cysteine knot peptides targeting sodium channels. Front Pharmacol. 2019;10:366.
22. Ahmad S, Khan H, Shahab U, Rehman S, Rafi Z, Khan MY, *et al*. Protein oxidation: An overview of metabolism of sulphur containing amino acid, cysteine. Front Biosci (Schol Ed). 2017;9:71-87.
23. Peskin AV, Meotti FC, Souza DLF, Anderson RF, Winterbourn CC, Salvador A. Intra-dimer cooperativity between the active site cysteines during the oxidation of peroxiredoxin 2. Free Radic Biol Med. 2020;158:115-25.
24. Han J, Liu H, Hu S, Qiu J, Yi D, An M, *et al*. Determination and correlation of the solubility of L-cysteine in several pure and binary solvent systems. Journal of Chemical & Engineering Data; c2020.
25. Desai M, Singh A, Pham D, Chowdhury SR, Sun B.

Discovery and visualization of the hidden relationships among N-glycosylation, disulfide bonds, and membrane topology. Int J Mol Sci; c2023, 24.
26. Rose J, Müller B, Groscurth S, Giese J, Eirich J, Finkemeier I, *et al*. The functionality of plant mechanoproteins (forisomes) is dependent on the dual role of conserved cysteine residues. Int J Biol Macromol. 2021;193:1332-9.
27. Shieh P, Hill MR, Zhang W, Kristufek SL, Johnson JA. Clip chemistry: Diverse (bio), (Macro) molecular and material function through breaking covalent bonds. Chem Rev. 2021;121:7059-121.
28. Jannatifar R, Parivar K, Hayati Roodbari N, Nasr-Esfahani MH. The effect of N-acetyl-cysteine on Nrf2 antioxidant gene expression in Asthenoterato-zoospermia men: A clinical trial study. Int J Fertil Steril. 2020;14:171-5.
29. Rajeeve K, Vollmuth N, Raman JS, Wulff TF, Baluapuri A, Dejure FR, *et al*. Reprogramming of host glutamine metabolism during Chlamydia trachomatis infection and its key role in peptidoglycan synthesis. Nat Microbiol. 2020;5:1390-402.
30. Ciosi M, Maxwell A, Cumming SA, Moss HDJ, Alshammari AM, Flower MD, *et al*. A genetic association study of glutamine-encoding DNA sequence structures, somatic CAG expansion, and DNA repair gene variants, with Huntington disease clinical outcomes. Biomedicine. 2019;48:568-80.
31. Yoo HC, Yu YC, Sung Y, Han JM. Glutamine reliance in cell metabolism. Exp Mol Med. 2020;52:1496-516.
32. Yoo HC, Park SJ, Nam M, Kang J, Kim K, Yeo JH, *et al*. A variant of SLC1A5 is a mitochondrial glutamine transporter for metabolic reprogramming in cancer cells. Cell Metab. 2020;31:267-83.e12.
33. Liu ZZ, Liu QH, Liu Z, Tang JW, Chua EG, Li F, *et al*. Ethanol extract of mulberry leaves partially restores the composition of intestinal microbiota and strengthens liver glycogen fragility in type 2 diabetic rats. BMC Complement Med Ther. 2021;21:172.
34. Kim CS, Ding X, Allmeroth K, Biggs LC, Kolenc OI, L'Hoest N, *et al*. Glutamine metabolism controls stem cell fate reversibility and long-term maintenance in the hair follicle. Cell Metab. 2020;32:629-42.e8.
35. Jara CP, Berti DAB, Mendes NF, Engel DF, Zanesco AM, Souza PDGF, *et al*. Glutamic acid promotes hair growth in mice. Sci. Rep. 2021;11:15453.
36. Muyinda IJ, Park JG, Jang EJ, Yoo BC. KRAS, a prime mediator in pancreatic lipid synthesis through extra mitochondrial glutamine and citrate metabolism. Int J Mol Sci; c2021, 22.

How to Cite This Article
Farag AES, Abdelsalam SF, Attar YAEL, Ibrahim RI, Neinaa YMEIH. Cysteine and Glutamine level in hair shaft fractures patients. International Journal of Dermatology, Venereology and Leprosy Sciences. Yy;vol(issue):pp.