The experience of infertility: A review of recent literature on POST TESTICULAR CAUSES OF MALE INFERTILITY

Comment [TI1]: This title can be re-phrased to capture what the author(s) are trying to discuss

UNDER PEER REVIEW

Abstract

Infertility is usually defined as the inability of a couple to conceive even after one year of unprotected, frequent sexual intercourse.[1,2] It affects about 15% of all couples in the United States and at least 180 million worldwide.[3,4] Male infertility is defined as the inability of a male to make a fertile female pregnant, also for a minimum of at least one year of unprotected intercourse. The male is solely responsible for about 20% and is a contributing factor in another 30% to 40% of all infertility cases.[5] As male and female causes often co-exist, it is important that both partners are investigated for infertility and managed together. Overall, the male factor is substantially contributory in about 50% of all cases of infertility[6,7,8]. More studies now place infertility within larger social contexts and social scientific frameworks although clinical emphases persist. Methodological problems remain but important improvements are also evident. We identify two vigorous research traditions in the social scientific study of infertility. One tradition uses primarily quantitative techniques to study clinic patients in order to improve service delivery and to assess the need for psychological counseling. The other tradition uses primarily qualitative research to capture the experiences of infertile people in a sociocultural context. We conclude that more attention is now being paid to the ways in which the experience of infertility is shaped by social context. We call for continued progress in the development of a distinctly sociological approach to infertility and for the continued integration of the two research traditions identified here.

Keywords: infertility, literature review, psychological distress, treatment, illness experience

Introduction;

There are multiple causes for male infertility, which can be broadly classified due to their general underlying etiology. These include endocrine disorders (usually due to hypogonadism) at an estimated 2% to 5%, sperm transport disorders (such as vasectomy) at 5%, primary testicular defects (which include abnormal sperm parameters without any identifiable cause) at 65% to 80% and idiopathic (where an infertile male has normal sperm and semen parameters) at 10% to 20%Certain toxin like lead and uric acid can ~~any~~ also lead to Infertility [9,10,11]The post testicular portion of the reproductive tract includes the epididymis, vas deferens, seminal vesicles, and associated ejaculatory apparatus.[12.13.14,15]

Comment [TI2]: Add reference

1. Cystic fibrosis: ~~;~~ Cystic fibrosis (CF) is the most common autosomal recessive genetic disorder in the United States and is fatal. It is associated with fluid and electrolyte abnormalities (abnormal chloride-sweat test) and presents with chronic lung obstruction and infections, pancreatic insufficiency, and infertility. Interestingly, 98% of men with CF have ~~are~~ missing parts of the epididymis. In addition, the vas deferens, seminal vesicles, and ejaculatory ducts are usually atrophic, or completely absent, causing obstruction. Spermatogenesis is usually normal.[16,17] Congenital absence of the vas deferens (CABVD) accounts for 1-2% of infertility cases. On physical examination, no palpable vas deferens is observed on one or both sides. As in CF, the rest of the reproductive tract ducts may also be abnormal and unreconstructable. This disease is related to CF. Even though most of these men demonstrate no symptoms of CF, up to 65% of patients will harbor a detectable CF mutation. In addition, 15% of these men will have renal malformations, most commonly unilateral agenesis.[17]

UNDER PEER REVIEW

2. Young syndrome:~~,~~Young syndrome presents with a triad of chronic sinusitis, bronchiectasis, and obstructive azoospermia. The obstruction is in the epididymis. The pathophysiology of the condition is unclear but may involve abnormal ciliary function or abnormal mucus quality.[77]Although spermatogenesis is usually normal, reconstructive surgery is associated with lower success rates than that observed with other obstructed conditions.[19]

Comment [TI3]: Is this a reference?

3. Idiopathic epididymal obstruction:~~,~~Idiopathic epididymal obstruction is a relatively uncommon condition found in otherwise healthy men. There is recent evidence linking this condition to CF in that one-third of men so obstructed may harbor CF gene mutations.[19,20]

4. Adult polycystic kidney disease; Adult polycystic kidney disease is an autosomal dominant disorder associated with numerous cysts of the kidney, liver, spleen, pancreas, epididymis, seminal vesicle, and testis. Disease onset usually occurs in the twenties or thirties with symptoms of abdominal pain, hypertension, and renal failure. Infertility with this disease is usually secondary to obstructing cysts in the epididymis or seminal vesicle.Obesity is another Causative factor for infertility with deranged lipid profile and ~~anf~~ Renal function test.[21,22]

5. Blockage of the ejaculatory ducts :~~,~~ Blockage of the ejaculatory ducts, the delicate, paired, collagenous tubes that connect the vas deferens and seminal vesicles to the urethra, is termed ejaculatory duct obstruction. It is the cause of infertility in 5% of azoospermic men. Obstruction can be congenital and result from mullerian duct (utricular) cysts, wolffian duct (diverticular) cysts, or congenital atresia or is acquired from seminal vesicle calculi or postsurgical or inflammatory scar tissue.[80]It presents as hematospermia, painful ejaculation, or infertility. The diagnosis is confirmed by finding a low-volume ejaculate and TRUS showing dilated seminal vesicles or dilated ejaculatory ducts. [23]

Comment [TI4]: Is this a reference?

UNDER PEER REVIEW

ACQUIRED BLOCKAGE

1. Vasectomy :-Itis performed on 750,000 men per year in the United States for contraception. Subsequently, approximately 5% of these men have the Vasectomy reversed, most commonly because of remarriage.[24]

2. Groin and hernia surgery :-It can result in inguinal vas deferens obstruction in 1% of cases. There has been concern that Marlex mesh used for hernia repairsmay add to perivasal inflammation and increase the likelihood of vasal obstruction.[25]

3. Bacterial infections:- Bacterial infections (E coli in men age > 35) or Chlamydia trachomatis in young men) may involve the epididymis, with scarring and obstruction.[22,25]

FUNCTIONAL BLOCKAGE

Besides physical obstruction, functional obstruction of the seminal vesicles may exist. Functional blockages may result from nerve injury or medications that impair the contractility of seminal vesicle or vasal musculature. A classic example of nerve injury affecting ejaculation is after retroperitoneal lymph node dissection for testis cancer. This can cause either retrograde ejaculation or true anejaculation, depending on the degree of injury to postganglionic sympathetic fibers arising from the thoracolumbar spinal cord. [26,27 ,28,29]These autonomic nerves overlie the inferior aorta and coalesce as the hypogastric plexus within the pelvis and control seminal emission. Multiple sclerosis and diabetes are other conditions that result in disordered ejaculation. Evidence from animal models indicates that the seminal vesicles, lined by smooth muscle, possess contractile properties similar to those of the urinary bladder, making it

UNDER PEER REVIEW

conceivable that seminal vesicle organ dysfunction may underlie some cases of ejaculatory duct obstruction.

GENETIC TESTING IN PATIENTS WITH AZOOSPERMIA

Genetic factors may play an important role in nonobstructive forms of azoospermia. The two most common categories of genetic factors associated with nonobstructive azoospermia are: a) chromosomal abnormalities resulting in impaired testicular function; and b) Y-chromosome microdeletions leading to isolated spermatogenic impairment.[29,30,31,32]

KARYOTYPE

A karyotype analyzes all chromosomes for the gain or loss of the entire chromosomes as well asstructural defects, including chromosome re-arrangements (translocations), duplications,deletions, and inversions. Chromosomal abnormalities account for about 6% of all maleinfertility, and the prevalence increases with increased spermatogenic impairment (severeoligospermia and nonobstructive azoospermia).[88] Paternal transmission of chromosome defectscan result in pregnancy loss, birth defects, infertility in male offspring, and other genomicsyndromes. Lead toxicity is one of the leading ~~laeding~~ causes of male infertility due to hazarderous effects on DNA due to microdeletions.[33,34,35]

Comment [TI5]: Which reference is this?

Y CHROMOSOME MICRODELETION

Approximately 13 % of men with nonobstructive azoospermia or severe oligospermia may havean underlying Y-chromosome microdeletion.[88,89,90] Y chromosome microdeletions responsible for infertility — regions AZF a, b, or c — are detected using sequence tagged sites (STS) andpolymerase chain reaction analysis. There is no consensus on the number of STS's

Comment [TI6]: Which references are these?

UNDER PEER REVIEW

required foroptimal detection of AZF deletions. Y chromosome microdeletions carry both prognosticsignificance for finding sperm and consequences for offspring if these sperm are utilized.

Successful testicular sperm extraction has not been reported in infertile men with large deletionsinvolving AZFa or AZFb regions but the total number of reports is limited.[91] However, up to80% of men with AZFc deletions may have retrievable sperm for ICSI. Furthermore, the couplemust be counseled on the inheritance of this compromised fertility potential in all maleoffspring.[36,37]

Comment [TI7]: Which reference is this?

Lifestyle Changes

Reasonable healthy lifestyle changes should be recommended or at least discussed with all male infertility patients. These changes include stopping smoking, limiting or eliminating alcohol intake, adopting a more nutritious diet, weight loss measures if obese, increased exercise, avoiding potentially toxic artificial lubricants during sexual activity, reducing stress, eliminating illegal and recreational drug use (such as marijuana), minimizing prescription drugs, avoiding exposure to pesticides and heavy metals (such as lead, mercury, boron, and cadmium), and eliminating any unnecessary chemical exposures.[29][30][36,37] Low body weight is also a possible risk factor for male infertility.[39,40,41] Fish oil ,almond oil , Fresh fruits containing antioxidants~~containingantioxidents~~supplements have also been suggested as helpful in male fertility, but there is insufficient evidence to make a recommendation.[42]

Depression and anxiety during pandemic COVID -19 have been ~~has~~ shown to worsen the quality of Life , might play a role in male infertility due to possible alterations in scrotal temperature, with being preferred, although the evidence is not compelling or definitive.[43,44]

Comment [TI8]: This sentence is not clear

UNDER PEER REVIEW

While avoiding hot baths, saunas, and tight-fitting underwear have ~~has~~ not been conclusively demonstrated to significantly improve male fertility, it is not unreasonable to discuss these suggestions with patients. Use of herbal medication,~~and~~ anti oxidant and various other healthy dietary planshave ~~has~~ been advocated ~~advised~~ by some studies.[45,46]Acquired urogenital abnormalities - bilateral obstruction or ligation of the vas deferens, bilateral orchiectomy, epididymitis, varicoceles, retrograde ejaculation.Immunological causes - lymphocytic hypophysitis, hemosiderosis, hemochromatosis, sarcoidosis, histiocytosis, tuberculosis, fungal infections, etc.Urogenital tract infections - Gonococci, chlamydia, syphilis, tuberculosis, recurrent urogenital infections, prostatitis, and recurrent ~~prostato~~prostate vesiculitis.[51.52.53] Sexual dysfunction - premature ejaculation, anejaculation, infrequent sexual intercourse, and erectile dysfunction.Malignancies - sellar masses, pituitary macroadenomas, craniopharyngiomas, and surgical or radiation treatment of ~~to~~ these conditions, testicular tumors, or adrenal tumors leading to an excess of androgens.Medications or drugs - cannabinoids, opioids, psychotropic drugs can cause inhibition of GnRH, exogenous testosterone or androgenic steroids supplementation, GnRH analogs and antagonists used in prostatic carcinoma, chronic glucocorticoid therapy, alkylating agents, antiandrogens, ketoconazole, cimetidine.Environmental toxins - insecticides, fungicides, pesticides, smoking, excess alcohol.While it remains unclear exactly how much influence these factors have in male infertility, it is reasonable to expect that avoiding potentially spermatotoxic activities and adopting a healthier lifestyle will improve overall male fertility.[54.55]

References

UNDER PEER REVIEW

1. Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss. Fertility and sterility. 2008 Nov:90(5 Suppl):S60. doi: 10.1016/j.fertnstert.2008.08.065. Epub
2. Khatoon F, Ibrahim ,Hafeezullah et al .Association of BMI with Follicular stimulating Hormone and with sperm parameters in males. IOSR Journal of Nursing and Health Science (IOSR-JNHS e-ISSN: 2320–1959.p- ISSN: 2320–1940 Volume 3, Issue 1 Ver. III (Jan. 2014), PP 13-23
3. Khatoon F et al .Correlation and reproductive hormone and fructose with sperm count and motility in infertile males. SAJMR Spectrum: A Journal of Multidisciplinary Research Vol. 3 Issue 5, May 2014
4. Khatoon F, Essaa Abdullah F , Mushtaq M , Balouch Z .Correlation of Fructose with Spermatogenesis. Pinnacle Biochemistry Research.Vol 1(1) 2014.
5. Khatoon F, AlamN, Mahmood A Imtiaz F,. Antisperms antibodies in infertile males attending a Tertiary Care Hospital in Karachi. Pak J Med Sci 2012;28(1):171-174
6. Khatoon F ,Mahmood A .Association Of BMI with Testosterone.Journal of the Dow University of Health Sciences Karachi 2012, Vol. 6 (2): 62-65.
7. Khatoon F at el. Association between BMI and Prolactin Levels in Male Patients Science Journal of Medicine and Clinical Trials. ISSN: 2276-7487 Volume 2013, Article ID sjmct-259, 6 Pages, 2012
8. Chuang WW, LoKC, Lipshultz LI, Lamb DJ. Male Infertility. In: Strauss III JF and Barbieri RL. (Eds) Yen and Jaffes Reproductive Endocrinology Elsievier, Saunders, Philadelphia, PA 2004; 669–90.
9. The World Health Organization (WHO). The SuRF Report 2: TheSurveillance of chronic disease Risk Factors. Geneva: WHO, 2005
10. Aboelnaga SM, F Kahtoon, R Hameed. Association between Serum Creatinine Kinase and Oral Submucousal Fibrosis. Bull. Env. Pharmacol. Life Sci., Vol 9[5] April 2020 : 125-127
11. Aboelnaga SM & Khatoon F. Effect of Mobile phone radiation on human health. Advances in Biotechnology and Microbiology, 16(1) 2020: 138-140. doi:10.19080/AIBM.2020.16.555926- ISSN 2474-7637
12. Alkwai H, Aboelnaga SM, Hussain RA, Kahtoon F. Surfactant protein D levels with obesity and type 2 diabetes mellitus [review article]. Gomal J Med Sci 2020 Jan-Mar;18(1):39-42. https://doi.org/10.46903/ gjms/18.01.2080 jan 2020
13. Khatoon F. Correlation of anti oxidant Zinc with Variousdiet pattern (Fructose oxonicacid ,fructose and oxonic acid) in induced Hyperuricemia. Advances In Bioresearch Vol 10(4) July2019
14. Khatoon F, F Aysha et al. Effect of Lead toxicity and correlation with different variables of DNA damages. JIDMC, journal of Islamabad medical and dental college Vol 7(2) May (2018)
15. Baker HWG, Barger HG, de Kretser D.M. Hudson B (1986). Relative incidence of etiologic disorders in male infertility. In: Male Reproductive Dysfunction: Diagnosis and Management of Hypogonadism, Infertility and Impotence. (Santen R J. Swerdloff R S Eds.), New York, Marcel Dekker, pp. 341-372.

16. Int J ObesRelatMetabDisord 2000 Apr;24(4):485-91 Vermeulen A. Senile hypogonadism in man and hormone replacement therapy. Acta Med Austriaca 2000;27(1):11-17.
17. (simony etall.1999) Simoni, M, Weinbauer, GF, Gromoll, J, Nieschlag. E. (1999). Role ofFSH in male gonadal function. Ann-Endocrinol-Paris, 60(2): 102-6
18. .Khatoon F , Essa F. Human Genetic Association Studies: association between of Human genome with Clinical outcome. Journal of Biotechnology and Microbiology..Vol 10.(1) 2018 ISSN :2474-7637
19. (karpas and Marrow) Morrow AF. Baker HWG, Burger HG (1986). Partial gonadotropin deficiency is infrequent in infertile men. Clin. Reprod. Fetil. 4: 319-327.
20. Karpas AE., Matsumoto AM., Paulsen CA., Bremmer MJ (1983): Elevated serum follicle-stimulation hormone levels in men with normal semen fluid analyses. FertilSteril, 39:333-336.
21. Vydra N, Malusecka E, JarzabMet al. Spermatocyte-specific expression of constitutively active heat shock factor 1 induces HSP70i-resistant apoptosis in male germ cells. Cell Death Differ. 13(2),212–222 (2006).
22. Khatoon F et al.Polymorphism Of Apolipoprotein B And Its Correlation With Adiposity. Spectrum: A Journal of Multidisciplinary Research Vol. 1 Issue 5, May 2014, ISSN 2278-0637, 180-191
23. Khatoon F et al.Polymorphism Of Apolipoprotein B And Its Correlation With Adiposity. Spectrum: A Journal of Multidisciplinary Research Vol. 3 Issue 5, May 2014, ISSN 2278-0637, 180-191(2014)
24. Raman J., D., Schlegal PH (2002). Aromatase inhibitors for male fertility. J Urol., 167(2 ntl): 624-9..(126)excess testosterone
25. Tuttelmann F, Gromoll J, Kliesch S. Genetics of male infertility. Urologe A. 2008 Dec;47(12):1561-2.
26. Reproductive Endocrinology and Infertility: Integrating Modern Clinical and Laboratory Practice .Douglas T. Carrell ,C. Matthew Peterson. Springer-Verlag .Pg 345-370.
27. Greil AL. Infertility and psychological distress: a critical review of the literature. Soc Sci Med 1997; 45:1679-1704.
28. Skakkebaek, Niels E, Giwercman, Aleksander, de Kretser, David . Pathogenesis and management of male infertility. Lancet Jun1994;343(8911): 1473-9
29. Khatoon F,Zahid B . Role Of Dietary Copper Supplementation As An Antioxidant In The Induced Hyper Uricemic Rat Model. Journal of international academic research for multidisciplinary, Volume 5, Issue 12, January 2018.ISSN; 2320-5083http://www.jiarm.com/JAN2018.
30. Khatoon F, Farhan Essa Abdullah. Human Genetic Association Studies: association between of Human genome with Clinical outcome. Adv Biotech & Micro. 2018; 10(1): 555778. DOI: 10.19080/AIBM.2018.10.555778
31. HendAlkwai ,Fahmida K. Significance And Role Of Genome Wide Association Studies In relation To Current Scenario Of Human Genomic Framework, Advances In Bioresearch, Volume 9 (6), Nov 2018.ISSN: 0976-4585 DOI: 10.15515/abr.0976-4585.9.6.163170]
32. Fahmida K .Use of Deoxy ribonucleic Acid in human identification. GomalJournal.of Medical Sciences,Volume 16 Oct-Dec 2018 ISSN: 1819-7973 https://www.pakmedinet.com/43017

33. Fahmida K, F Aysha et al. Effect of Lead toxicity and correlation with different variables of DNA damages. JIDMC ,2018 (7)2. PG 102-107
34. Ahmad F., Pervez A., Khatoon F., Ahmed Z., Mahmood S., 2014. Correlation of serum lead with various hematological parameters in male humans (car painters) of Lahore. International Journal of Biochemistry. Photon 195, 388-394. Impact Index: 4.52, e. ISSN: 4438-5728:
35. Fozan Ahmed, Ayesha Pervez, Fahmida Khatoon. Association of Lead with Heamoglubin damage in males (car painters) of Lahore. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 13, Issue 1 Ver. IX. (Feb. 2014), PP 83-88
36. Meyerhardt JA, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Nelson H,Whittom R, Hantel A, Thomas J, Fuchs CS. Impact of body mass indexand weight change after treatment on cancer recurrence and survival inpatients with stage III colon cancer: findings from Cancer and LeukemiaGroup B 89803. J Clin Oncol 2008; 26:4109–4115.
37. Khatoon, F., Mahmood, M. R., Obeidat, S. T., Alsatti, M. A. M., Alanazi, R. S. S. A., Kabbos, R. S. M. A., Balouch, Z., &Obelanga, S. M. H. (2021). Assessment of Perception, Awareness about Predictors of Colorectal Cancer of Hail Region Saudi Arabia population. Journal of Pharmaceutical Research International, 32(47), 14-24. https://doi.org/10.9734/jpri/2020/v32i4731108
38. Khatoon F et al. Challenges linked with adherence to treatment by adult TB patients in Pakistan.IOSR P-ISSN:2279-086. PP-40-45
39. Aboelnaga SM, BalouchFk.Protective Effect of Yerba Mate on Rats Fed on High Cholesterol Diet- An Experimental Study.J Clin of Diagn Res.2021; 15(10):BC09-BC13. https://www.doi.org/10.7860/JCDR/2021/47930/15499
40. Shimaa M A ,Fahmida K. Dietary habits and consumption of fruits and vegetables in type 2 Diabetes in Ha'il Saudi Arabia. Bull. Env. Pharmacol. Life Sci., Vol 9[5] 2020 : 05-11
41. Awadh Al-Hazimi1, FahmidaKhatoon.Strategies for Preventive measure and awareness tools for COVID-19 and for adherent stress and anxiety, Advances In Bioresearch, Volume 11(13), May 2020 pg 54-62.ISSN: 0976-4585 http://soeagra.com/abr/abr_may2020/8.pdf
42. Kahtoon, F., Ahmed, R. M. E., Iqbal, N., Balouch, Z., &Alenazi, F. S. (2021). Genetic Identification: A Review on Autosomal Single Nucleotide Polymorphism's as Diagnostic Tool for Identifying Human. Journal of Pharmaceutical Research International, 32(46), 25-33. https://doi.org/10.9734/jpri/2020/v32i4631099
43. Zahra A, Hassan S-u-N, Hassan MS, Parveen N, Park J-H, Iqbal N, Khatoon F and Atteya MR (2022) Effect of physical activity and sedentary sitting time on psychological quality of life of people with and without disabilities; A survey from Saudi Arabia. Front. Public Health 10:998890. doi: 10.3389/fpubh.2022.998890
44. Hassan SU, Zahra A, Parveen N, Khatoon F, Bangi NA, Hosseinzadeh H. Quality of Life and Adherence to Healthcare Services During the COVID-19 Pandemic: A Cross-Sectional Analysis. Patient Prefer Adherence. 2022 Sepdoi: 10.2147/PPA.S378245. PMID: 36147381; PMCID: PMC9488595
45. Zakout YM, Khatoon F, Bealy MA, Khalil NA, Alhazimi AM. Role of the Coronavirus Disease 2019 (COVID-19) pandemic in the upgrading of personal hygiene. A cross-

sectional study in Saudi Arabia. Saudi Med J. 2020 Nov;41(11):1263-1269. doi: 10.15537/smj.2020.11.25402
46. Aboelnaga SM & Khatoon F. (2020) Effect of Jerusalem Artichoke and Olive Oil on Hyperglycemic Rats. J Genet Cell Biol, 4(1): 207-216. https://www.scitcentral.com/article/26/1746/Effect-of-Jerusalem-Artichoke-and-Olive-Oil-on-Hyperglycemic-Rats#tabs6
47. Aboelnaga, S. M. H., & Khatoon, F. (2021). Effect of Low Fat Diet, lmonds, Green Coffee and Mackerel Fish on Obese Rats. Journal of Pharmaceutical Research International, 32(42), 80-89. https://doi.org/10.9734/jpri/2020/v32i4231058
48. KhatoonF , Awadh Al-Hazimi1. Pandemic COVID -19 comparative analysis with MERSA and SARS , Etiology epidemic and current Interventions with future prospective, Advances In Bioresearch, Volume 11(13), May 2020 pg 31-36.ISSN: 0976-4585
49. Khatoon F ,HendAlkwai et al .Preventive measure and Use of Herbal medicine for COVID -19 Bulletin of Environment, Pharmacology and Life Sciences Bull. Env. Pharmacol. Life Sci., Vol 9[6]2020. Pg 18-22 ISSN: 277-1808 ISI indexed journal published 9/5/2020
50. Aboelnaga, S. M. H., & Khatoon, F. (2021). Analyzing the Impact of Long-Lasting Changes in Energy Homeostasis and Nutrient Sensing on Nutritional Programming of Hypothalamus in Rats. Asian Journal of Medicine and Health, 18(12), 32-38. https://doi.org/10.9734/ajmah/2020/v18i1230283
51. Fahmida K. Recent Techniques Based on the Utilization of DNA and Autosomal Single Nucleotide Polymorphism. Gomal Journal of Medical Sciences,Volume 16 April-June 2019 Vol 17,NO 2. Pg 59-62 ;ISSN: 1819-7973 https://www.pakmedinet.com/journal/53/1/June/2019/17(2)
52. Khatoon F, Yahya RS, et al. (2014) Natural Regulatory T Cells in Some Parasitic Diseases. J BacteriolParasitol 6: 210. doi:10.4172/2155-9597.1000210 ISI indexed journal
53. 61. Shizabatool, Fahmida k at el . Lowered serum metal levels in fructose-induced hyperuricaemic rat model. The National Medical Journal Of India Vol. 28, NO. 3, 2015
54. Sarwar Beg, Waleed Hassan Almalki, Fahmida Khatoon, Arshi Malik, Sarah Afaq, Hani Choudhry.Lipid- and polymer-based nanocomplexes in nucleic acid delivery as cancer vaccines,Drug Discovery Today,2021,ISSN 1359-6446

Comment [TI9]: The references should follow the same pattern. Some of the references are old, they can be changed to more recent references.

UNDER PEER REVIEW