

# Study of the prevalence of azoospermia in patients with Hodgkin's lymphoma prior to treatment

Azarm Taleb, Azarm Hoda<sup>1</sup>, Azarm Arezoo, Jalilian Mahshid

Department of Oncology, Medical School, Isfahan University of Medical Sciences, <sup>1</sup>Department of Biology, Isfahan University, Isfahan, Iran

## Abstract

**Background:** Infertility is one of the main problems of patients with Hodgkin's lymphoma, as this causes specific effects in the social, family, and emotional life of patients. Hodgkin's lymphoma is a neoplastic disorder that comprises of 0.6% of all cancers and often occurs in middle-aged people, with a mean age of 26 years. It originates from neoplastic changes in the lymphoid cells, which lead to different complications in the body organs. One important complication of Hodgkin's lymphoma is humoral and cellular immune system dysfunction that can cause numerous and dangerous problems for patients. Another complication of Hodgkin's lymphoma is sterility, more specifically hypogonadism and azoospermia. Sterility may appear after treatment. Considering that most patients with Hodgkin's lymphoma have a good survival, diagnosing and treating this complication and preventing its incidence contributes to improving the quality of social life and emotional status of these patients.

**Materials and Methods:** In this study, 238 patients whose Hodgkin's lymphoma was approved by Pathology were included in the study, before receiving any medical intervention, and they were examined for sterility (sperm status). Sterility of the male patients was confirmed using a spermogram test. The serum levels of the luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone (T) were checked.

**Results:** Among the studied patients, 24 patients (10.08%) suffered from azoospermia, which was evident in its progressive stages.

**Conclusion:** In such cases, treatment of Hodgkin's lymphoma and improvement of the immune system could overcome azoospermia and sterility.

**Key Words:** Azoospermia, hodgekin's lymphoma, prevalence

## Address for correspondence:

Dr. Azarm Taleb, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: azarm@med.mui.ac.ir

Received: 02.10.2012, Accepted: 26.11.2012

## INTRODUCTION

Hodgkin's lymphoma is a neoplastic disorder

arising from the lymphoid cells and diagnosed on the basis of a pathological study of the tissue suspected of the disease, by observing the Reed-Sternberg cells and connective tissue in a study of tissue sections. The classical Hodgkin's disease has four histopathological subtypes, which are as follows:<sup>[1,2]</sup>

Lymphocyte-predominant Hodgkin's lymphoma (LPHL)  
Nodular sclerosis Hodgkin's lymphoma (NSHL)  
Mixed cellularity Hodgkin's lymphoma (MCHL)  
Lymphocyte depletion Hodgkin's lymphoma (LDHL)

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.115803

Copyright: © 2013 Taleb. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**How to cite this article:** Taleb A, Hoda A, Arezoo A, Mahshid J. Study of the prevalence of azoospermia in patients with Hodgkin's lymphoma prior to treatment. Adv Biomed Res 2013;2:73.

Each pathological subtype of Hodgkin's lymphoma has its own manifestations and symptoms. The histological subtype has a partial effect on the treatment and prognosis of the disease. Male patients show worse prognosis than female patients.

Hodgkin's lymphoma is a neoplastic disease that threatens a patient's life if it grows rapidly. Late diagnosis of the disease can have serious outcomes, which may be irreparable. A delayed diagnosis results in progress of the disease, and consequently, more invasive methods will be needed to control it.<sup>[2,3]</sup>

Infertility refers to the inability of a couple to reproduce over one year of sexual intercourse, without using contraceptive means.

Male infertility is caused by different factors including endocrine abnormalities, epigenetic changes, and genetic mutations. In many cases, identifying the cause of infertility and treating it results in the continuation of marriage and mental relief for the couple.

Sterility may exist in patients several years before appearance of the clinical symptoms of Hodgkin's lymphoma. Primary hypogonadism is usually distinguished from secondary hypogonadism by measuring the serum levels of LH and FSH. In case of primary hypogonadism, the serum levels of LH and FSH increase and the serum level of testosterone and the sperm count decrease.<sup>[4]</sup> The present study examines patients with Hodgkin's lymphoma in terms of azoospermia before any medical intervention [Table 1].

## MATERIALS AND METHODS

In this study, the infertility of 238 patients with Hodgkin's lymphoma was examined. They did not receive any chemotherapy, or radiotherapy, and were being examined to discover the stage of the disease. Female patients were excluded from the study due to lack of certain facilities to prove their sterility. Sterility of male patients was confirmed using the spermogram test. The serum levels of LH, FSH, and testosterone were checked. The

present study was performed from 1999 to 2009, in Isfahan's Hazrat-e-Seyedoshohada Center, affiliated to the School of Medicine, in the Isfahan University of Medical Sciences. The patients were asked about their experiences of the disease and probable infertility symptoms, including the state of the testes when touched, status of the secondary sexual characteristics, hair growth, patient's sexual behavior in the past, any history of radiation, previous surgical operations and medication, family history, and secondary disorders of infertility. If there was any doubt about the patients' experiences of the disease and clinical symptoms, they were examined through a pelvic and testes ultrasound examination or urology consultation. Subsequently, a fasting blood sample was taken and delivered to the laboratory of the same center, to measure the serum levels of LH, FBS, and testosterone. Almost 10 weeks after medical intervention and complete remission of the disease, the patients underwent a spermogram again and the results were recorded and examined.

All the spermograms were carried out by one person in one laboratory. The spermogram examined the following factors: Volume of the sperm and seminal fluid, sperm count in a cubic centimeter, percentage of motile sperm in a microscopic field, percentage of deformed, abnormal, dead, and tailless sperms and sperm components, white blood cell and red blood cell count in the blood sample, and abnormal cell infiltration.<sup>[5,6]</sup> All the patients were examined in periodical follow-ups for five years, after complete remission.

## RESULTS

In this study, 238 patients with Hodgkin's lymphoma in the age range of 18-52 years were examined. Among these patients, 24 patients (10.08%) were affected with azoospermia before receiving any chemotherapy or radiotherapy. An analysis of the number of patients with azoospermia, based on the histopathological subtypes, revealed that LDHL was more common than the other subtypes [Table 2].

The percentage of azoospermia in advanced stages (III and IVB) was more than that in the moderate

**Table 1: Duration of sterility by month, before diagnosis of Hodgkin's Lymphoma**

Patients	Duration of sterility (month)	Percentage
Five patients	16	20.83
Three patients	24	12.5
Six patients	30	25
Six patients	36	25
Four patients	42	16.66

**Table 2: Percentage of azoospermia based on the pathological subtypes of Hodgkin's Lymphoma**

Number and type of Hodgkin's pathology	Number of the patients	Number of azoospermia	Percentage of azoospermia
Lymphocyte Predominant	30	2	6.66
Nodular sclerosis	57	5	8.77
Mixed type	92	11	11.95
Lymphocyte depletion	59	8	13.55

stages (I and IIA) of the disease [Table 3]. Moreover, oligospermia, obvious reduced sperm motility, and teratospermia were observed frequently. However, there was no hypospermia and aspermia.

### Specifications of the spermogram

The sperm volume of 14 samples was less than 1 cc and 10 samples had a sperm volume of 1-2 cc. The percentage of motile sperm in 20 samples was less than 10%, and four and three samples comprised of 20 and 30%, respectively.<sup>[5,6]</sup>

There were 10-15 motile sperms in each microscopic field. The number of spermatozoa in all the patients was less than 40 million per cubic centimeter, and the deformed and dead spermatozoa increased noticeably.

The results of the hormone analysis of LH, FSH, and testosterone were in the normal range in all patients. On the basis of the above-mentioned results, the azoospermia of the patients could not be attributed to primary and secondary testicular failure; however, it could be attributed to immune and autoimmune disorders like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

## DISCUSSIONS

According to the clinical observations and experiences and also global publications, hypogonadism and sperm disorders were observed in certain cancers.<sup>[7]</sup> In the present study, 10.08% of the patients with Hodgkin's lymphoma suffered from gonadal failure, before medical intervention. The results showed that Hodgkin's lymphoma could cause infertility. The mechanisms by which Hodgkin's lymphoma caused gonadal failure were not clear.<sup>[8,9]</sup> Although the initial gonadal damage was not important and could be due to hypothalamus-pituitary axis failure, it was more likely due to the humoral and cellular immune system, and consequently, incidence of an autoimmune disorder against the spermatozoa; however, it could be reduced by controlling the disease and by complete remission.<sup>[10]</sup> The type of

medications used by the patients was of special importance, as some chemotherapy drugs could result in sterility.

After chemotherapy, especially along with an MOPP (Mustin, Oncovine, Procarbazine and Prednisone) diet or similar diets, testicular dysfunction is seen in almost all patients (more than 90%) and spermatogenetic recovery is seen only in 20% of the patients (9b). The rate of testicular damage depends on the number and dosage of the drug and frequency of chemotherapy. If the three-course therapeutic protocol of MOPP is restricted, the azoospermia will be moderate and spermatogenetic recovery will be possible after some months. However, in most cases, more chemotherapeutic courses are needed to control the disease completely. Azoospermia is considerably reduced when no combined treatment with alkylating agents or procarbazine is applied.<sup>[9,10]</sup> When using an ABVD (Adriamycine, bleomycine, Vinblastine and Decarbazine) diet, azoospermia is seen in 36% of the cases and spermatogenetic recovery is seen in all patients (100%).<sup>[10,11]</sup> The gonadal toxicity reaches a minimum when using the VMB (vinblastine, Bleomycin, and methotrexate) diet.

Secondary sterility, which occurs following chemotherapy, is the result of initial testicular damage. Although FSH increases, spermatogenetic recovery may not happen. Therefore, determining the level of FSH alone is not enough to prove recovery.<sup>[12,13]</sup> In general, young men with Hodgkin's Lymphoma suffer an underlying gonadal dysfunction.

The study of 15 patients with azoospermia, 10 weeks after termination of chemotherapy (along with an ABVD diet), showed that three patients recovered, one patient recovered six months after treatment, and another patient who was unsatisfied with undergoing the spermogram test after chemotherapy, gained his fertility after 14 months (based on the pregnancy of his wife). Going by the above-mentioned results, it can be concluded that azoospermia underlies Hodgkin's Lymphoma, and this may be due to autoimmune reasons, and may be treated or reduced after a while using an appropriate treatment. Azoospermia is mostly seen in the advanced stages of Hodgkin's Lymphoma and can be used as a prognostic factor to detect the progress of the disease and deterioration of the patient's status.<sup>[14-15]</sup>

Among the studied patients, 24 patients with azoospermia underwent chemotherapy or radiotherapy or both. Ten weeks after termination of the treatment, a spermogram and measurement of the LH, FSH, and testosterone serum levels were carried out again, and

**Table 3: Percentage of azoospermia based on Hodgkin's Lymphoma stages**

Staging	Number of the patients	Number of azoospermia	Percentage of azoospermia
I and IIA	8	-	0
IIIA	41	1	2.43
I and IIB	41	6	14.36
IIIA	33	3	9.09
IIIB	57	7	12.28
IVB	58	9	15.51

it was revealed that 15 patients had recovered from azoospermia.<sup>[16]</sup>

## REFERENCES

1. Rosenberg SA. The management of Hodgkin's disease: Half a century of change. The Kaplan Memorial Lecture. *Ann Oncol* 1996;7:555-60.
2. Helman D. Rosenberg's. *Cancer Principles and Practice of Oncology*. 9th ed. New York: Lippincott Williams and Wilkins; 2011.
3. Bojesen A, Juul S, Birkebaek NH, Gravholt CH. Morbidity in Klinefelter syndrome: A Danish register study based on hospital discharge diagnoses. *J Clin Endocrinol Metab* 2006;91:1254-60.
4. Meirou D, Schenker JG. Cancer and male infertility. *Hum Reprod* 1995;10:2017-22.
5. Sigman M, Baazeem A, Zini A. Semen analysis and sperm function assays: What do they mean? *Semin Reprod Med* 2009;27:115-23.
6. Berman M, Englewood Cliffs NJ. Male Infertility Best Practice Policy Committee Members and Consultants. American Urological Association; American Society for Reproductive Medicine. 2001.
7. M'kacher R, Bennaceur-Griselli A, Girinsky T, Koscielny S, Delhommeau F, Dossou J, et al. Telomere shortening and associated chromosomal instability in peripheral blood lymphocytes of patients with Hodgkin's lymphoma prior to any treatment are predictive of second cancers. *Int J Radiat Oncol Biol Phys* 2007;68:465-71.
8. Schover LR, Brey K, Lichtin A, Lipshultz LI, Jeha S. Knowledge and experience regarding cancer, infertility, and sperm banking in younger male survivors. *J Clin Oncol* 2002;20:1880-9.
9. Behringer K, Breuer K, Reineke T, May M, Nogova L, Klimm B. Secondary amenorrhea after Hodgkin's lymphoma is influenced by age at treatment, stage of disease, chemotherapy regimen, and the use of oral contraceptives during therapy: A report from the German Hodgkin's Lymphoma Study Group. *J Clin Oncol* 2005;23:7555-64.
10. Rueffer U, Breuer K, Josting A, Lathan B, Sieber M, Manzke O. Male gonadal dysfunction in patients with Hodgkin's disease prior to treatment. *Ann Oncol* 2001;12:1307-11.
11. Chapman RM, Sutcliffe SB, Malpas JS. Male gonadal dysfunction in Hodgkin's disease. A prospective study. *JAMA* 1981;245:1323-8.
12. Ragni G, Bestetti O, Santoro A, Viviani S, Di Pietro R, De Lauretis L. Evaluation of semen and pituitary gonadotropin function in men with untreated Hodgkin's disease. *Fertil Steril* 1985;43:927-30.
13. Viviani S, Ragni G, Santoro A, Perotti L, Caccamo E, Negretti E. Testicular dysfunction in Hodgkin's disease before and after treatment. *Eur J Cancer* 1991;27:1389-92.
14. van der Kaaij MA, van Echten-Arends J, Simons AH, Kluin-Nelemans HC. Fertility preservation after chemotherapy for Hodgkin lymphoma. *Hematol Oncol* 2010;28:168-79.
15. Harel S, Fermé C, Poirot C. Management of fertility in patients treated for Hodgkin's lymphoma. *Haematologica* 2011;96:1692-9.
16. Dohle GR. Male infertility in cancer patients: Review of the literature. *Int J Urol* 2010;17:327-31.

**Source of Support:** Isfahan University of Medical Sciences, **Conflict of Interest:** No.