

# CORRELATION OF FOLLICLE STIMULATING HORMONE AND LUTEINISING HORMONE WITH TESTICULAR SPERM BIOPSY RESULT

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## ABSTRACT

**Objective:** To investigate the correlation of follicle stimulating hormone (FSH) and luteinising hormone (LH) with testicular sperm biopsy result in azoospermia patients. **Material & methods:** This is a cross sectional descriptive analytic study. Data were collected from medical record in Klinik Permata Hati Sardjito General Hospital Yogyakarta. We divided them into two groups, sperm group and non-sperm group of sperm biopsy result. We recorded the level of FSH and LH pre-operation. The results were expressed as mean  $\pm$  standard deviation (SD). The correlation coefficient (r) between various parameters was determined by analysis for Spearman's rank correlation test. **Results:** We found 35 patients who met the inclusion and exclusion criteria during 2010-2012, who performed testicular biopsy, age range between 28-44 yo. The mean of FSH on sperm group (12.75 mIU/mL) was higher than non-sperm group (7.26 mIU/mL). The mean of LH on sperm group (5.8 mIU/mL) was also slightly higher than non-sperm group (5.70 mIU/mL). We found weak correlation between FSH level and testicular biopsy ( $r = 0.095$ ), while on LH level was found negative correlation with testicular biopsy ( $r = -0.053$ ). There were 42.85% patients with negative sperm result within normal range of FSH and 100% with normal range of LH. The Level of FSH with positive result ranged between 1.94-19.7 mIU/mL and LH level with positive result were 1.38-17.69 mIU/mL. **Conclusion:** FSH and LH were important plasma hormones correlated with spermatogenesis. FSH level between 1.94-19.7 mIU/mL and LH level between 1.38-17.69 mIU/mL could be used as reliable criteria for testicular sperm biopsy.

**Keywords:** Follicle stimulating hormone, luteinising hormone, testicular sperm biopsy, azoospermia.

## ABSTRAK

**Tujuan:** Untuk mengetahui korelasi antara kadar follicle stimulating hormone (FSH) dan luteinising hormone (LH) dengan hasil biopsi sperma testis pada pasien azoospermia. **Bahan & cara:** Penelitian ini adalah analisa deskriptif silang. Data dikumpulkan dari rekam medis Klinik Permata Hati RSUD Dr. Sardjito Yogyakarta. Kami membagi mereka dalam 2 kelompok, kelompok sperma dan kelompok non-sperma dari hasil biopsi sperma. Kami mencatat level FSH dan LH sebelum operasi. Hasil menunjukkan rerata  $\pm$  standard deviation (SD). Koefisien korelasi (r) antara berbagai parameter dihitung menggunakan analisa tes korelasi Spearman's rank. **Hasil:** Kami mencatat 35 orang pasien dengan kriteria inklusi dan eksklusi selama Maret 2010 sampai Agustus 2012, yang dilakukan biopsi testis dengan umur antara 28-44 tahun. Rerata level FSH pada kelompok sperma (12.75 mIU/mL) lebih tinggi dari kelompok non-sperma (7.26 mIU/mL). Rerata LH pada kelompok sperma (5.8 mIU/mL) juga sedikit lebih tinggi dari kelompok non-sperma (5.70 mIU/mL). Kami menemukan korelasi yang lemah antara level FSH dan biopsi testis dengan  $r = 0.095$ , sementara level LH ditemukan korelasi negatif dengan biopsi testis ( $r = -0.053$ ). Terdapat 42.85% pasien dengan hasil sperma negatif dalam range FSH normal dan 100% dengan range LH normal. Level FSH dengan hasil positif antara 1.94-19.7 mIU/mL dan level LH dengan hasil positif 1.38-17.69 mIU/mL. **Simpulan:** FSH dan LH adalah hormon plasma yang penting berkaitan dengan spermatogenesis. Level FSH antara 1.94-19.7 mIU/mL dan level LH antara 1.38-17.69 mIU/mL dapat digunakan sebagai kriteria yang dapat dipertanggungjawabkan untuk biopsi sperma testis.

**Kata kunci:** Follicle stimulating hormone, luteinising hormone, biopsi sperma testis, azoospermia.

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## INTRODUCTION

Infertility is defined as inability to conceive within one year of sexual activity without

contraceptive use.<sup>1</sup> World Health Organization (WHO) defined infertility as a sexually active couple who are unable to have spontaneous pregnancy within one year.<sup>2</sup> 15% of couples that did not have

pregnancy within 1 year and seek for medical treatment. 5% of infertility patients failed to have a birth. Men has 50% contribution to infertility. Male infertility can be acquired in some conditions such as congenital defect, urogenital tract infection, increasing of scrotum temperature (varicocele), endocrine disturbance, genetic failure, immunology factor.<sup>1,2</sup>

All men with suspicion of infertility must have semen analysis. Men with azoospermia must be followed with reproductive hormone evaluation, Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH).<sup>3</sup> Serum FSH and LH are used to determine testis function. If azoospermia caused by testis failure, it will increase reproductive hormones, because failure of testis to produce inhibin hormone to suppress FSH and LH level to normal. High FSH level has been used to diagnose primary testis failure, that seminiferous tubulus in testis can not produce sperm normally. High FSH level can not define testis damage, partial or total. Its mean that man with high FSH level might have some normal testis area that can produce sperm. This sperm might be used to infertility treatment with testis biopsy or Intra Cytoplasmic Sperm Injection (ICSI). Low FSH is rare that usually caused by hypogonadotropic hypogonadism.<sup>3,4</sup>

One of man reproduction organ is testis consist of more than 900 seminiferous tubuli. There are Leydig cell in seminiferous tubuli, which function to produce androgen hormone, testosterone. Evaluation of testosterone level can give information about testis that can produce testosterone. Most of infertile man have normal testosterone level, because compartment which sperm is produced differs from testosterone.<sup>3</sup>

FSH and LH are primary pituitary hormones that regulate testis function. Both of it are glycoprotein consisting of 2 sub-unit polypeptide chains,  $\alpha$  and  $\beta$ , each of them coded by different genes. FSH and LH produced by gonadotropin cell at hipofisis glands on anterior lobe, that target cell is testis (seminiferous tubuli). FSH stimulates sperm production that work on testosterone receptor at seminiferous tubuli and LH stimulates Leydig interstitial cell in testis to secrete testosterone hormone.<sup>4,5</sup>

Testis biopsy is used to evaluate the infertility. In general, biopsy technique used small incision on scrotum wall and tunica albuginea. Defect on seminiferous tubuli and cell composition can be assessed and categorized in few pattern. Testis

biopsy is most useful in azoospermia patients. Indication of testis biopsy is to determine that men with testis atrophy, testis failure and high FSH level has mature sperm that can be used to IVF or ICSI. Single testis biopsy can detect sperm on 30% man with azoospermia, high FSH level and testis atrophy. Sperm from testis origin can be collected and recently is used to solve problem of man with infertility. Testis biopsy can determine that some patient have a dead end to overcome their infertility problem and must be informed not to seek another medical treatment.<sup>6,7</sup>

## OBJECTIVE

The aim of this study is to get correlation between FSH and LH level with testis biopsy on patients with azoospermia. Second objective is to get FSH and LH cut off value to predict testis biopsy result.

## MATERIAL & METHOD

This is a cross sectional descriptive analytic study. Data were collected from medical record in Klinik Permata Hati Dr. Sardjito General Hospital in Yogyakarta from years of 2010-2012. We divided them into two groups with sperm group and non-sperm group of sperm biopsy result. We recorded the level of FSH and LH pre operation. The number samples taken in this research was 35 patient. Inclusion criteria is patients with azoospermia who underwent testicle biopsy. Exclusion criteria is patient performed biopsy for other causes. The results were expressed as mean  $\pm$  standard deviation (SD). The correlation coefficient (r) between various parameters was determined by analysis for Spearman's rank correlation test.

## RESULTS

This study found 35 patients who met the inclusion and exclusion criteria during the years 2010-2012 with an age range 27-62 years. FSH and LH examinations were performed on patients whose testicular biopsy contain sperm and does not contain

**Table 1.** Characteristic levels of FSH and LH.

Variable	Maximum	Minimum	Mean (median)
FSH level	1.94	28.8	9.93 (7.7)
LH level	1.38	17.69	6.97 (5.34)

sperm. The mean level of FSH with positive sperm on biopsy is 12.75 mIU/ml, while in the group with negative sperm was 7.26 mIU/ml. (Fig. 1)

Mean LH levels in patients with positive sperm was 5.8 mIU/ml, while in the group with negative sperm was 5.7 mIU/ml. (Fig. 2)

The largest age group of patients in this study is 15 people in the range of 31-35 years, followed by 8 people aged 26-30 years, none of the patients was under 25 years of age, and there were 3 patients over 45 years old. Patients in this study had a fairly good level of education, all patients were high school graduates with 28 people educated D IV/Bachelor, 4 people were III diploma and 3 people

were post graduate. Javanese is an ethnic majority of patients in this study, the number is 25 people. The rest are Chinese, Sundanese, Batak, Balinese, Minang and 2 patients came from abroad.

In this study, it was found that there is a weak correlation between the levels of FSH with testicular biopsy with  $r = 0.095$  and a negative correlation between the levels of LH in testicular biopsies with  $r = -0.053$ . (Figure 3 and 4)

A total of 42.85% of patients had negative sperm biopsy results with normal FSH levels and 100% with normal LH levels. FSH levels with positive biopsy results ranged from 1.94-19.7 mIU/ml and LH levels 17.69-1.38 mIU/ml.

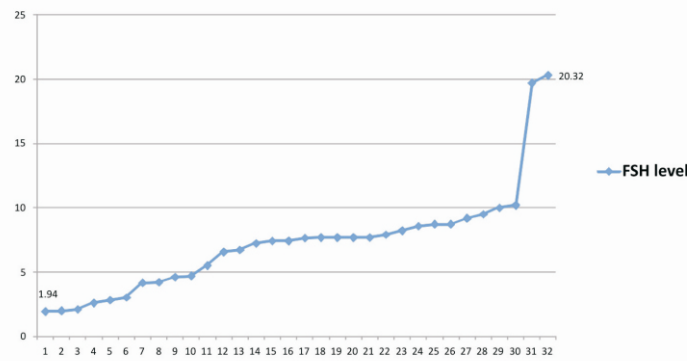


Figure 1. Level of follicle stimulating hormone (FSH).

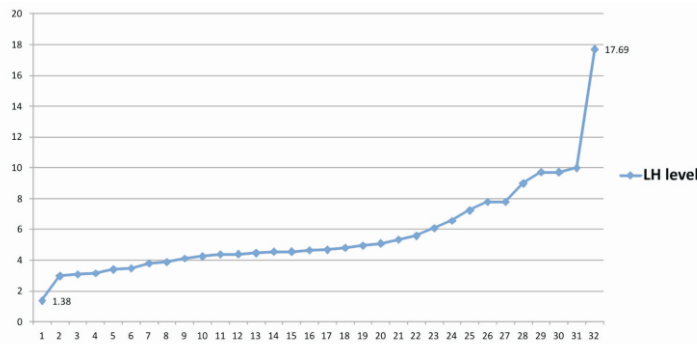


Figure 2. Level of luteinizing hormone (LH).

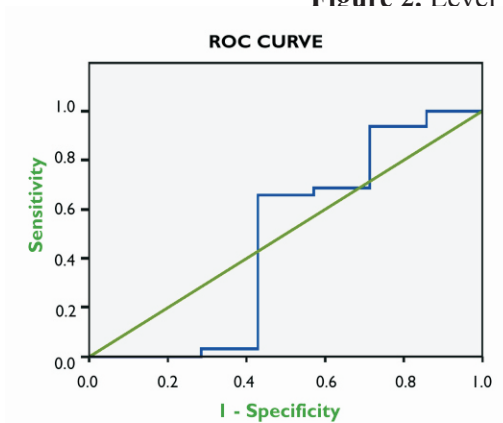


Figure 3. Sensitivity and specificity of FSH.

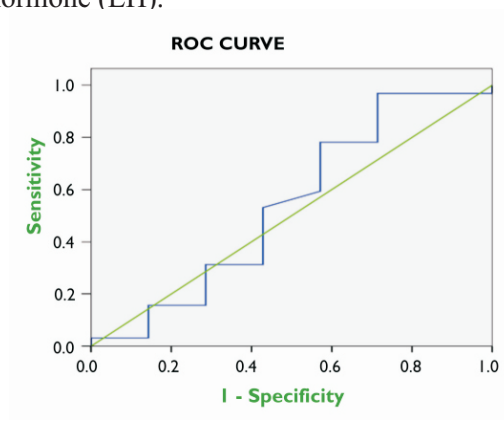


Figure 4. Sensitivity and specificity of LH.

## DISCUSSION

Testicular biopsy has 2 functions in the management of infertility in men. First, this procedure is used as a diagnostic tool to differentiate the anatomic pathology of infertility due to obstruction or non-obstructive and as a therapy to retrieve good sperm for ICSI. Testicular biopsy has 2 functions in the management of infertility in men. First, inspection is used as a diagnostic tool to differentiate the anatomic pathology of infertility due to obstruction or non-obstructive and as a therapy to take good sperm for ICSI. Testicular biopsy is indicated for patients with obstructive azoospermia (normal testicular size and normal FSH levels). Testicular biopsy is considered normal if > 85% of testicular volume consists of seminiferous tubules, mature germ cells, and Sertoli cells, the rest is made up of blood vessels and Leydig cells in the interstitial tissue. Spermatogenesis starts from the formation of spermatogonia to spermatocytes in the basal membrane and finally located in the lumen tubulus.<sup>8</sup>

Normal FSH level is 1.7 to 12 mUI/ml.<sup>9</sup> Increased FSH levels occurred in patients with abnormal spermatogenesis and Sertoli cell dysfunction due to inadequate inhibition of negative feedback by inhibin. Increased FSH > 7.6 mUI/ml with testicular axial length of < 4.6 cm had a 89% probability to be non-obstructive azoospermia, but normal FSH levels does not always guarantee normal spermatogenesis.<sup>10</sup> Normal LH levels are 5-10 mUI/mL.<sup>11</sup> Luteinizing hormone (LH) is a hormone that stimulates the Leydig cells to produce testosterone, which then will be used to spermatogenesis process.<sup>8</sup>

Recent indications of testicular biopsy is to determine whether the men suffering from testicular atrophy, testicular failure, and elevated levels of FSH, have mature sperm that can be used for IVF and ICSI. Single testicular biopsy can detect the presence of sperm in 30% of men with azoospermia, increased levels of FSH and testicular atrophy. Sperm derived from testes obtained from biopsies are now routinely used to help men with male factor infertility to become a father.<sup>6</sup>

In this study, we found 35 patients who met the inclusion and exclusion criteria during the years 2010-2012 with an age range 27-62 years, highest number of patients were in the age range 30-35 years of 15 people. Patients generally have a pretty good level of education, in this study all patients had at

Diploma level III or more. Javanese is the majority ethnic of patients in this study is, the number of 25 people The rest are Chinese, Sundanese, Batak, Balinese, Minang and 2 patients who came from abroad the country. FSH and LH examination performed on infertile patients with testicular biopsy results were positive sperm and which are not. The mean FSH levels in patients with positive sperm was 12.75 mIU/ml, while in the group with negative sperm 7.26 mIU/ml. (Chart 1). The mean LH levels in patients with positive sperm was 5.8 mIU/ml, while in the group with negative sperm 5.7 mIU/ml (Chart 2). Geidam AD et al conducted a study on hormonal influences on male infertility in Nigeria. In the study obtained sample with range of age between 22-52 years. Of the 96 patients with azoospermia, normal FSH was found in 29.2%, high in 66.7%, and low in 4.1% with an average value 20.70 mIU/ml, whereas normal LH levels found in 54.2%, high in 45.8% and low in 0% with an average value 12.87 mIU/ml. When compared with this study, the average levels of FSH and LH in patients with biopsy testicular results negative sperm is lower than previous reported research.<sup>11</sup>

Ziae et al reported levels of FSH in patients with sperm positive biopsy results were  $5.83 \pm 3.51$  and negative were  $20.82 \pm 5.85$  and LH levels with biopsy results sperm positive  $8.04 \pm 6.31$  and negative  $9.06 \pm 0.53$ . Ziae et al showed FSH hormone levels were better than LH levels in predicting biopsy results.<sup>12</sup> Compared with this study, there are differences in the levels of FSH where average values with positive sperm is higher than the negative. It can be caused due to small sample in this study. Whereas for LH levels an average value is nearly equal between positive and negative sperm.

In this study, there was weak correlation between the levels of FSH by testicular biopsy with  $r = 0.095$  and a negative correlation between the levels of LH in testicular biopsies with  $r = -0.053$ . (Chart 3 and 4). A total of 42.85% of patients had negative sperm biopsy results with normal FSH levels and 100% with normal LH levels. FSH levels had positive biopsy results ranged from 1.94 to 19.7 mIU/ml and LH levels 1.38-17.69 mIU/ml.

FSH along with LH is the primary pituitary hormones that regulate testicular function. Both are glycoproteins consisting of 2 sub-unit polypeptide chains, namely  $\alpha$  and  $\beta$ , each encoded by a separate gene.<sup>13,14</sup> FSH and LH are produced by gonadotropin cells in the anterior lobe of the pituitary gland with

the target cell in testis (seminiferous tubules) where FSH functions to stimulate the production of sperm by affecting testosterone receptors in the seminiferous tubules and LH stimulates the interstitial Leydig cells of the testes to secrete testosterone.<sup>3,15</sup>

Testicular biopsy is useful to evaluate infertility because it can precisely determine the clinical diagnosis of multiple disorders of infertility. Disorders of the seminiferous tubules and cell composition may be assessed and categorized into several patterns. Testicular biopsy is most useful in patients with azoospermia.<sup>4,5,16</sup>

## CONCLUSION

FSH levels which has positive biopsy results ranged between 1.94-19.7 mIU/mL. LH levels which has positive biopsy results between 1.38-17.69 mIU/mL. FSH and LH is an important plasma hormone related to spermatogenesis.

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