

# Seminal Anti-Mullerian Hormone in Fertile and Infertile Men

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## Abstract

**Objective:** Anti-Mullerian hormone (AMH) is a glycoprotein of the transforming growth factor  $\beta$ -superfamily, is produced by Sertoli cells and have been proposed as direct marker of their function and indirect marker of spermatogenesis.

The aim of this study is to demonstrate that serum and seminal AMH as non-invasive marker of spermatogenesis in infertile men and to find the relationship between seminal AMH, FSH, LH, prolactin and testosterone.

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**Setting:** Al-Batool Teaching Hospital and Al-Duaa clinical lab.

**Design :** prospective study.

**Participants and Methods:** The study was conducted on seventy male subjects aged less than fifty years for the period from Sept2012-Feb2013. Infertile men were classified into azoospermics (n=20), oligospermics (n=20), and fertile men as controls (n=30).

Serum concentrations of FSH, LH, prolactin and testosterone were measured using ELISA.

Serum AMH and AMH in seminal plasma concentrations were measured using AMH/MIS enzyme immunoassay sorbant kit.

**Results:** Infertile men had lower seminal and serum AMH levels and was statistically significant. There was a significant negative correlation between seminal AMH and FSH in azoospermic men while no significant correlation was found with LH, prolactin and testosterone.

Concerning oligospermic men, a significant positive correlation was found between seminal AMH and testosterone while no significant correlation was found with FSH, LH and prolactin.

**Conclusion:** the present study found that AMH in seminal plasma can be used as indirect marker of infertility in men.

**Keywords:** Male infertility, Seminal AMH.

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## Introduction

Infertility is a problem that affects more than 10-15% of couples during reproductive

years and male factor infertility is the cause of half of the cases<sup>(1)</sup>. Most male factor infertilities are due to testicular failure which results in a decline in semen quality<sup>(2)</sup>.

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Seminal plasma results from a mixture of various secretions from different parts of the male reproductive organs, less than 10% of the seminal plasma results from the seminiferous tubules and the epididymis<sup>(3)</sup>.

Seminal plasma contains Anti-Mullerian hormone (AMH) which is produced by Sertoli cells in the seminiferous tubules<sup>(4,5)</sup>.

Anti-Mullerian hormone expression and secretion by Sertoli cells is regulated by inhibitory paracrine actions of intratesticular testosterone and neighboring germ cells and by a stimulating hormonal effect of follicle stimulating hormone<sup>(5,6)</sup>.

Anti-Mullerian hormone is a member of the transforming growth factor  $\beta$ -(TGF- $\beta$ ) super family of glycoprotein<sup>(7,8)</sup>.

In human, large amounts of AMH are produced during fetal and post natal testicular development<sup>(9)</sup>.

Anti-Mullerian hormone is secreted by the apical pole of the Sertoli cells toward the lumen of the seminiferous tubules, resulting in higher concentration of AMH in the seminal plasma than in the serum<sup>(10)</sup>.

Serum AMH is a marker of Sertoli cell activity in boys, and its decline during puberty may be interpreted as an early sign of local T-activity and spermatogenic activities in the testes<sup>(5)</sup>.

Although the function of AMH in post natal life is incompletely understood, AMH has been reported to control Leydig cell proliferation and steroidogenesis<sup>(11)</sup> and may also be related to germ cell differentiation<sup>(12)</sup>, therefore, evaluation of the biochemical characteristics of semen provide valuable non-invasive biomarkers for evaluating the function of the seminiferous tubules.

The aim of the present study is to demonstrate that serum and seminal AMH as non-invasive markers of persistent

spermatogenesis in azoospermic and oligospermic men and to find the relationship between seminal AMH, FSH, LH, prolactin and testosterone.

### **Participants and Methods**

The study was carried out on seventy subjects attending the male infertility clinic at Al-Batool Teaching Hospital in Mosul for the period between Sept2012-Feb2013, and informed consent was obtained from all subjects before entry into the study.

Twenty infertile azoospermic men recruited for this study (mean age 32.65±8.11 years) and twenty infertile oligospermic men were included in the study (mean age 33.2±4.58 years), the control population consisted of thirty fertile men (mean age 27.3±5.75 years).

Hormone estimation was done at Al- Duaa clinical lab.

Serum and seminal AMH levels were measured using AMH/MIS enzyme linked immune sorbent assay kit.

Serum concentrations of FSH, LH, prolactin and testosterone were measured using ELISA.

### **Statistical Analysis**

It was carried out using Minitab Version13. Descriptive statistics, mean and standard deviation (SD) were given for the data.

A p-value  $\leq 0.05$  was considered significant.

Unpaired t-test was used to compare means of serum level of hormones in azoospermics, oligospermics and controls.

Unpaired t-test was used to compare means of serum AMH and AMH in seminal plasma of fertile and infertile men.

Relationships between AMH in seminal plasma and various hormones were evaluated by Spearman correlation coefficient.

**Results**

Table 1 shows that infertile men had lower levels of semen AMH when compared with control men and it was statistically significant, the 95% confidence for difference: (1.719;

2.672) .

Concerning serum AMH, also there was a significant difference between infertile men and controls, 95% confidence for difference (1.369; 2.394).

**Table 1. Comparison between mean serum and seminal AMH levels in fertile and infertile men**

Parameter	Infertile men (n=40)	Fertile men(n=30)	p-value
Seminal AMH ng/ml	1.932±0.92	4.13±1.04	0.000
Serum AMH ng/ml	1.91±1.29	3.797±0.85	0.000

\* unpaired t-test was used

Table 2 depicts a significant decrease in seminal AMH in azoospermic men as compared to controls. 95% confidence for difference: (-2.880; -1.730).

Also a significant decrease in serum AMH in azospermics as compared to controls. 95% confidence for difference: (-2.875; -1.978).

Decreased seminal AMH in oligospermic men was found when compared with fertile men and statistically significant.

95% confidence for difference (-2.647; -1.533).

Also a significant decrease in serum AMH in oligospermics as compared to fertile men. 95% confidence for difference: (-2.100; -0.573).

**Table 2. comparison of mean serum AMH, seminal AMH levels in azoospermics, oligospermics and controls**

parameter	Azoospermic men (n=20)	Oligospermic men (n=20)	Controls (n=30)	p-value
Seminal AMHng/ml	1.825±0.952	2.040±0.900	4.13±1.04	0.000
SerumAMH ng/ml	1.370±0.711	2.46±1.61	3.797±0.853	0.000

\* unpaired t-test was used.

Fig. 2. demonstrates a significant negative correlation between seminal AMH and FSH in azoospermic men, while no significant

correlation was seen between seminal AMH, LH, prolactin and testosterone as shown in Fig. 1,3,4.

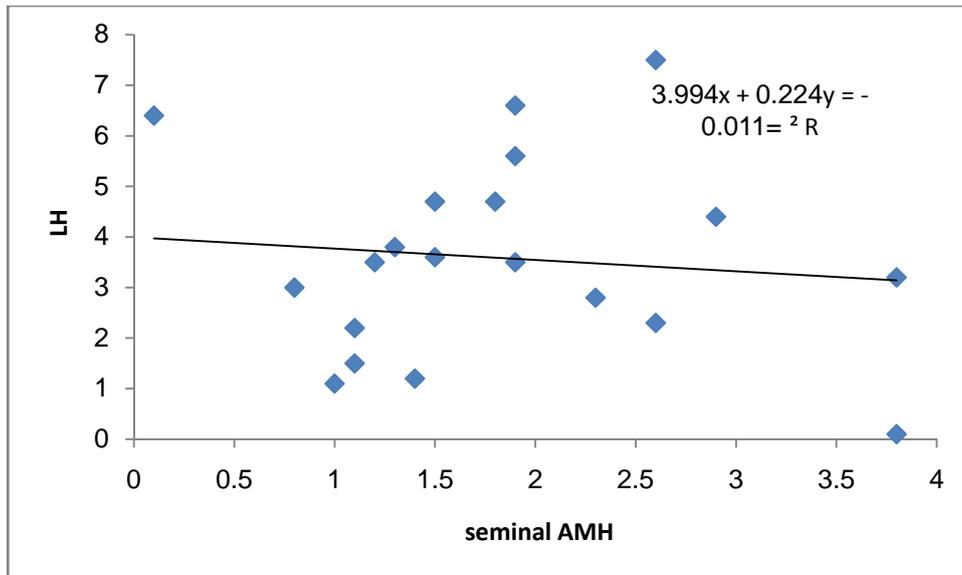


Fig. 1: Correlation between seminal AMH & serum LH in azoospermic men

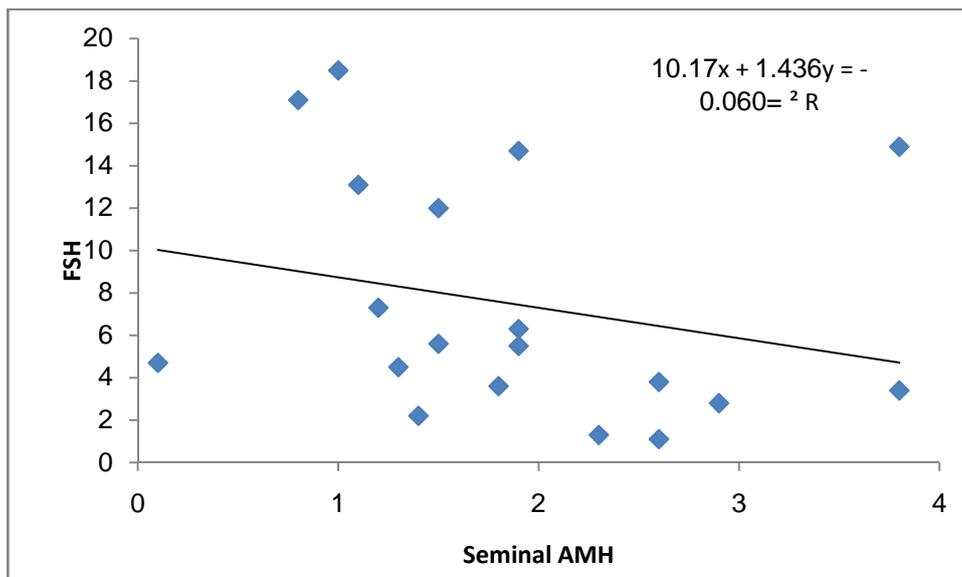
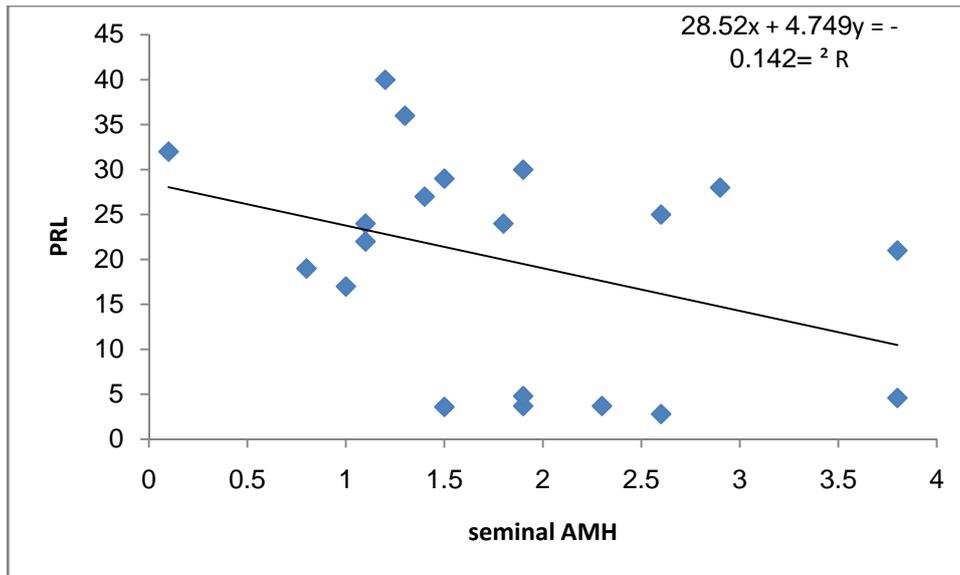
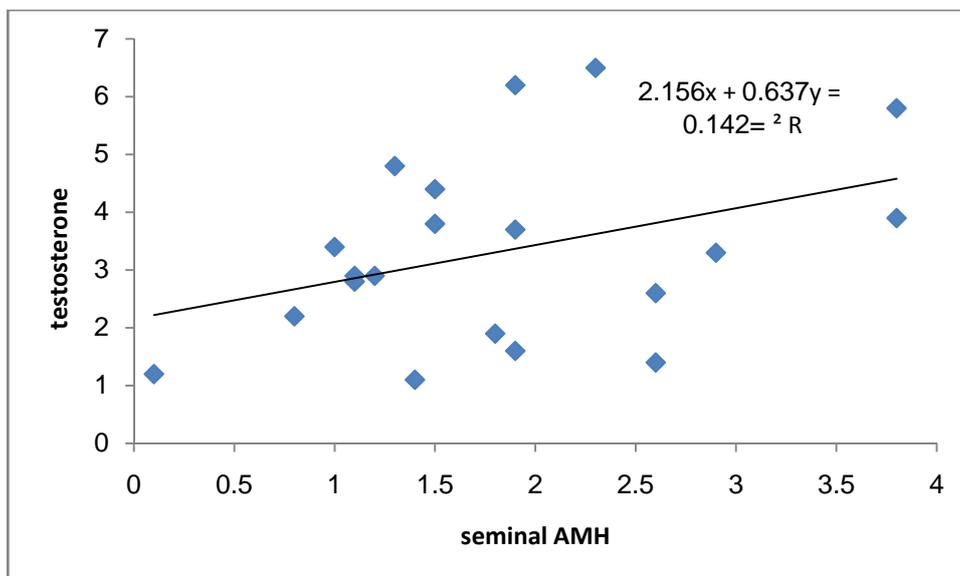


Fig. 2: Correlation between seminal AMH & serum FSH in azoospermic men



**Fig. 3: Correlation between seminal AMH & serum prolactin in azoospermic men**



**Fig. 4: Correlation between seminal AMH & serum testosterone in azoospermic men**

Fig 8. demonstrates a significant positive correlation between seminal AMH and testosterone in oligospermic men while no significant correlation between seminal AMH and FSH, LH, prolactin as shown in Fig. 5,6,7.

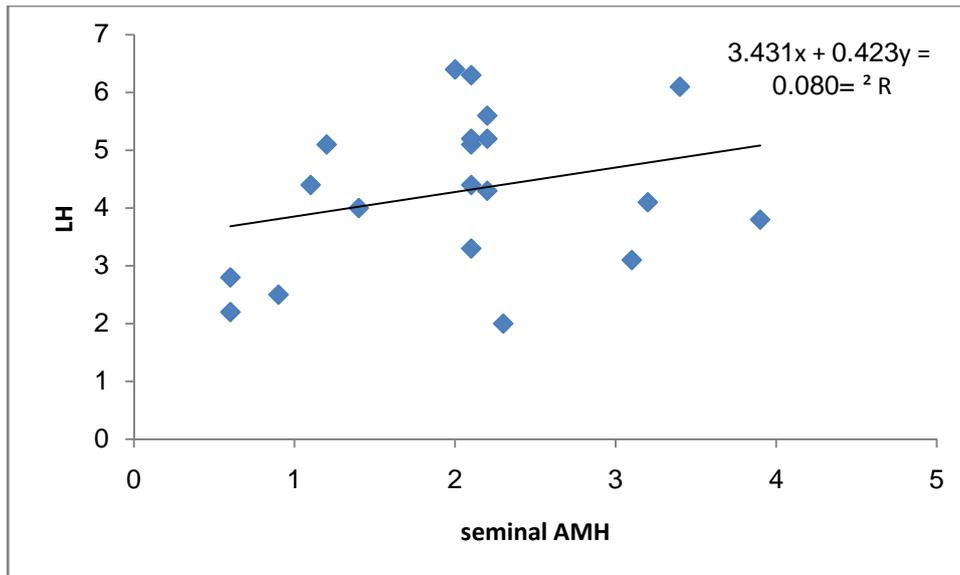


Fig. 5: Correlation between seminal AMH & serum LH in oligospermic men

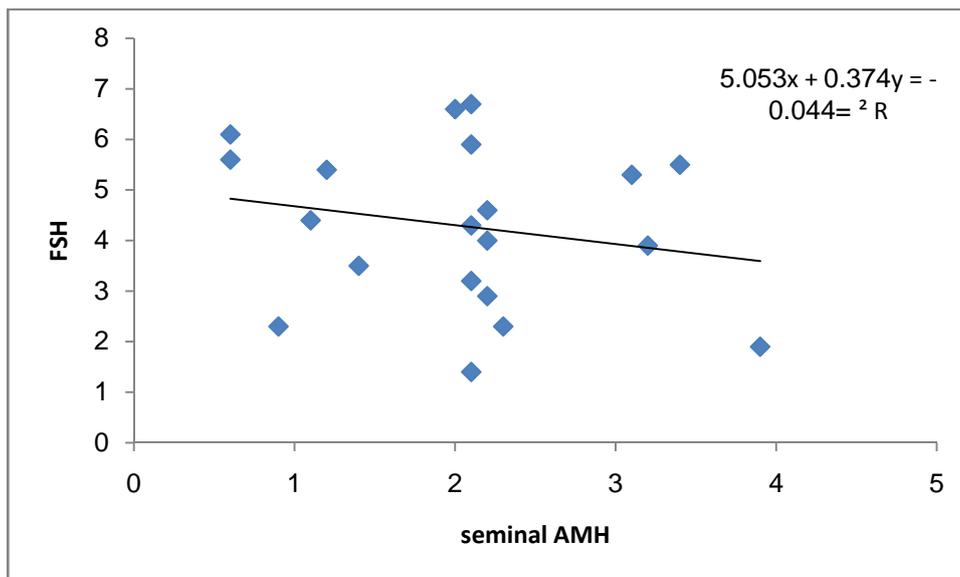


Fig. 6: Correlation between seminal AMH&serum FSH in oligospermic men

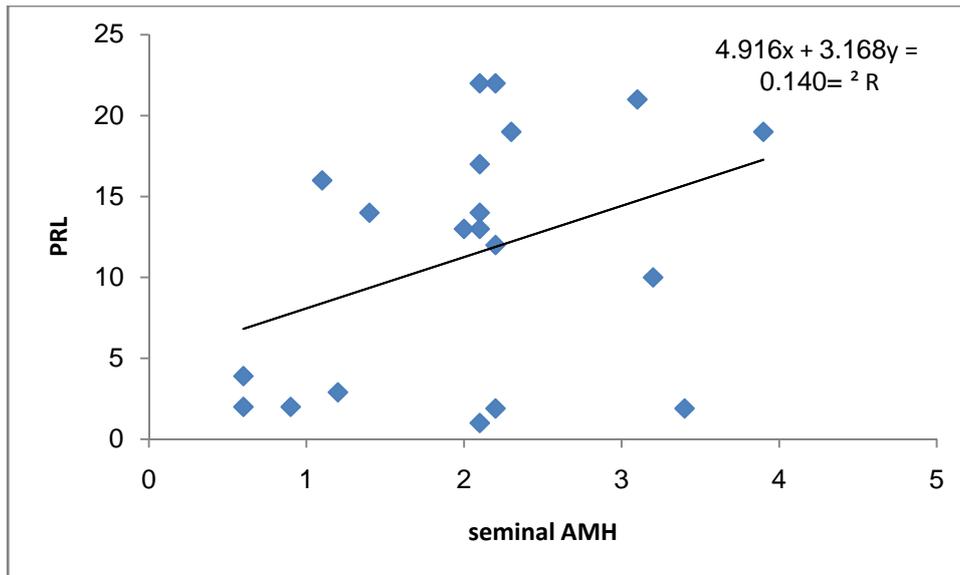


Fig. 7: Correlation between seminal AMH serum prolactin in oligospermic men

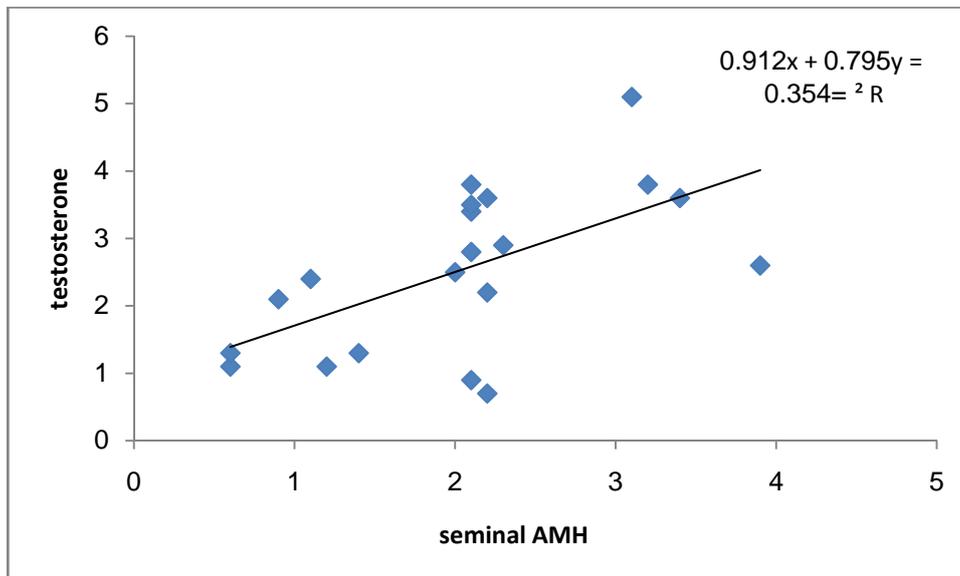


Fig. 8: Correlation between seminal AMH & serum testosterone in oligospermic men

### Discussion

Several studies with questionable results have focused on the value of serum FSH and inhibin to predict the status of spermatogenesis in the testes of azoospermic men, but the number of papers concerning the potential significance of seminal biomarkers of

spermatogenesis are very little<sup>(13)</sup>.

The present study compared spermatogenesis biomarkers in seminal plasma in normospermic (fertile), oligospermic and azoospermic men. The results showed that seminal AMH significantly lower in infertile men compared with fertile men, this is in

agreement with other authors<sup>(4,14,15)</sup>.

Similarly serum AMH have been found to be lower in infertile men as compared with fertile men and this is in agreement with other studies<sup>(16,17,18)</sup>. This reveals close correlation between AMH concentration and progress in spermatogenesis<sup>(10,15)</sup>.

In azoospermic men seminal AMH was found to be significantly negatively correlated with serum FSH level and this disagrees with Fenichel P *et al* 1999<sup>(10)</sup> but our study agrees with Sabetian S *et al* 2010<sup>(4,13,19)</sup>. Serum LH, prolactin and testosterone not correlated significantly with AMH concentration in seminal plasma and this in agreement with Fujisansa 2002<sup>(4)</sup>.

Seminal plasma AMH was found to be significantly lower in oligospermic men as compared to fertile men and this in agreement with Mostafa *et al* 2007<sup>(14)</sup>.

In oligospermic men seminal AMH was

found to be not correlated with FSH, LH and prolactin while it was significantly positively correlated with testosterone as AMH have been reported to control Leydig cell proliferation and steroidogenesis<sup>(11)</sup>.

Concerning the results of this paper, all of them are in agreement with other authors as mentioned in the discussion **except** that about the correlation between seminal AMH & FSH in azoospermic men, only one literature disagrees with our results and this was done in 1999 while our result was in agreement with more recent studies as mentioned in the discussion as the literature in 2010, & probably this is the explanation.

In conclusion AMH in seminal plasma may be important for sperm production and is a good marker for male infertility.

In addition, the clinical importance is the prediction of success of testicular sperm extraction in non obstructive azoospermia.

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## هورمون انتي- موليرين المنوي في الرجال الخصيبين والعقيمين

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### الملخص

**الهدف:** الهدف من الدراسة هو توضيح إذا كان بالإمكان استخدام هرمون انتي موليرين في السائل المنوي كعلامة لتكوين النطف في الرجال العقيمين، وكذلك لمعرفة العلاقة بين هرمون انتي موليرين في السائل المنوي والهرمون المحفز للحريب، الهرمون اللوتيني، هرمون التستوستيرون وهرمون الحليب.

**طريقة العمل والمشاركين:** أجريت الدراسة على سبعين رجلاً معدل أعمارهم أقل من خمسين سنة للفترة من أيلول 2012- شباط 2013.

تم تصنيف الرجال العقيمين حسب عدد النطف إلى مجموعة انعدام النطف، ومجموعة قلة النطف وكذلك شملت الدراسة ثلاثين رجلاً خصيباً كعينة سيطرة.

تم قياس تركيز هرمون انتي موليرين في مصل الدم وفي السائل المنوي كما تم قياس تركيز الهرمون المحفز للحريب، الهرمون اللوتيني، هرمون الحليب وهرمون التستوستيرون بواسطة جهاز ELISA.

**النتائج:** أظهرت النتائج اختلاف مهم في تركيز هرمون انتي موليرين في مصل الدم والسائل المنوي عندما تمت مقارنتهم بين الرجال الخصيبين والرجال العقيمين.

كذلك لوحظ علاقة عكسية بين هرمون انتي موليرين والهرمون المحفز للحريب في الرجال العقيمين مجموعة انعدام النطف، بينما لم يلاحظ علاقة مهمة مع تركيز الهرمون المحفز للحريب، الهرمون اللوتيني، هرمون الحليب، وهرمون التستوستيرون.

بخصوص مجموعة قلة النطف، لوحظ علاقة طردية بين هرمون انتي موليرين وهرمون التستوستيرون، بينما لم يلاحظ علاقة مع الهرمون المحفز للحريب، الهرمون اللوتيني وهرمون الحليب.

**الاستنتاج:** وجدت الدراسة الحالية أن هرمون انتي موليرين ممكن استخدامه كعلامة غير مباشرة للعقم عند الرجال.

**الكلمات الدالة:** عقم الرجال، هرمون انتي موليرين في السائل المنوي.