

How to Increase Female Fertility with Very Low AMH?

Leila Soudah*

German Board Certified Specialist in Obstetrics and Gynecology, Dubai, United Arab Emirates

Abstract: We reported a case of a 33-year-old woman who was married for five years, had low anti-mullerian hormone (AMH) and had four years of primary infertility. The aim was to produce eggs over many cycles, acquire several embryos, and freeze them to increase the pregnancy rate with a holistic approach. In this case, women who have given up hope of having children may find renewed optimism; nevertheless, conventional medical training only goes so far. The new paradigm emphasises a patient-centered, holistic approach that optimises the patient's body in each case with their own experience.

Keywords: AMH anti-mullerian hormone, Case report, Female infertility, Infertility, Functional medicine, Holistic approach.

1. Introduction

Despite research showing the relevance of the mind and body connection to fertility, the therapeutic practice has neglected the psychological elements of infertility [1, 2]. Clinical surveillance, hormone therapies, and in vitro fertilization (IVF) place mental, financial, and emotional strains on women and their spouses. If conceiving is difficult, a couple will be frustrated and disappointed [3, 4]. Around 180 million couples in developing nations have infertility due to main or secondary causes, according to statistics from the World Health Organization [5]. Nevertheless, if the problems continue and the man or woman is labeled as having reproductive issues, this may severely damage sanity, physical health, and self-assessed sexuality [6]. However, Alfred Jost identified the anti-mullerian hormone (AMH) in the 1940s and explained its significance in embryonic gender determination [7]. It has also been shown to affect ovarian function, particularly follicle development [8]. Independent groups have recently evaluated AMH's ability to predict live birth; preliminary results suggested that AMH might be employed as a prognostic factor [9, 10]. However, the data needed to provide definitive answers on AMH's predictive usefulness at low or very low concentrations. The effectiveness of ovarian reinvigoration and stimulation has improved the development of various therapeutic processes and methods [11]. Melatonin has also been used as an antioxidant and enter infertility supplement in recent years [12]. Melatonin is a tryptophan-serotonin-derived indoleamine. Melatonin is a special indole amine found throughout the body despite its unusual tiny size and lipophilic nature. It has several biological effects, from bacterial to mammalian [13]. The pineal gland in

the brain produces the hormone melatonin, which is subsequently released into the bloodstream. Light inhibits the pineal gland's melatonin synthesis, whereas darkness stimulates its production [14, 15]. It protects against oxidative stress-induced molecular mutilation and cellular malfunction in the ovary and placenta [16]. Melatonin also decreases oxidative stress by scavenging reactive oxygen species (ROS) and increasing endogenous antioxidant enzymes [17, 18]. Indoleamine modulates biological rhythms, reproduction, immunological response [19]-[21] and more, in addition to its anticancer [22, 23] and metabolic actions [24, 25]. Indoleamine improves gametes, culture media, luteal function, and embryos, making it a potential fertility control tool [26]-[29]. Melatonin administration during ovarian stimulation has been studied [26, 30, 31]. Therefore, the objective was to attempt to gather eggs throughout several cycles, to get multiple embryos, and to freeze them to boost the pregnancy rate using a holistic approach and using bioidentical melatonin orally and other mineral and vitamin supplements since a high amount of Gonatropine hormone would not be effective in this case.

2. Case Presentation

Here we present a case of a 33-year-old woman who was married for five years, and had low anti-mullerian hormone (AMH) and elevated Prolactin. She visited Dr. Leila 'Soudah's clinic for the first time on 17/12/20. She never used birth control. Therefore, her tubes were patent. Her family history revealed hypertension, Diabetes mellitus, and CVDs. She had a sedentary lifestyle. Also, she was a smoker who drank alcohol thrice a week. Initial gynaecological investigation showed that during the final four years of her marriage, she saw several physicians, took a great deal of medicine and attempted IUI once without result. Her spouse was previously married and had one kid.

In such situations, we must pose the inquiry. An effort was made to examine almost every inch of her body and optimise her vitamins, minerals, and hormones. Vital signs showed Weight 70.0 kg, Height 172 cm, BMI 23.6, Temp 36.5 C, Pulse 79 bpm, BP 100/60 mmHg. Regional examination (Head to Toe Approach) was unremarkable. Her ferritin level was very low, 29.01, and her vitamin D level was insufficient for a safe pregnancy, which must be between 60. She slept poorly,

*Corresponding author: drleilasoudah1@outlook.com

primarily late at night. Her Zinc levels were subpar, and her Homocysteine levels were excessive. Her free testosterone level was greater than average. Her Ultrasound revealed less active ovaries on both sides, corresponding to a low AMH level (Figure 1).

Keeping her condition in view, multiple laboratory assessment was carried out during the first visit, as shown in table 2 that, includes Vaginal ultrasound (Figure 2), Hormones Test (second cycle day), Anti-Muller Hormone (AMH) levels, Fasting Blood Tests, Vitamin D, and zinc Test. Upon further examination, it was observed that the patient's fasting glucose was slightly raised due to her late bedtime. Her vitamin and mineral levels were balanced and her lifestyle was modified prior treatment. Inositol was administered to reduce it to 85 mg/dl because even a number over 85 will raise diabetes risk by 6%. Another mineral administered was Zinc, as Zinc is essential for the production of DNA.

Approximately 3000 proteins bind to zinc to preserve the shape and integrity of ribosomal RNA and DNA methylation. A woman needs at least 8 mg of zinc per day. Zinc is essential for egg fertilisation and the regulation of ovulation, and

deficiency reduces egg quality. Zinc is required by more than 300 enzymes and is necessary for cell metabolism. Zinc regulates hormone action to facilitate ovulation and gastrointestinal inflammation. Vitamin D was also induced in the patient to help reduce sugar and insulin levels. In our case, optimizing her insulin and glucose levels was essential. Other than these necessary minerals, the patient was prescribed supplements with specific doses for a certain duration, as shown in Table 1.

In addition to treating her hip and muscular discomfort, homocysteine was crucial for her infertility. It has been observed that hyperhomocysteinemia is a risk factor for unexplained infertility and pregnancy loss [32]. As a result of its relationship with placenta vasculopathy, elevated homocysteine affects egg quality and recurrent pregnancy loss [33, 34].

The first treatment cycle we chose was a low responder protocol consisting of Clomid 150 mg and Growth hormone 4 IU. It has been reported that GH improves egg quality and embryo implantation. GH has been used in IVF since 1980 [35]. There is strong evidence that adding GH to a high stimulation

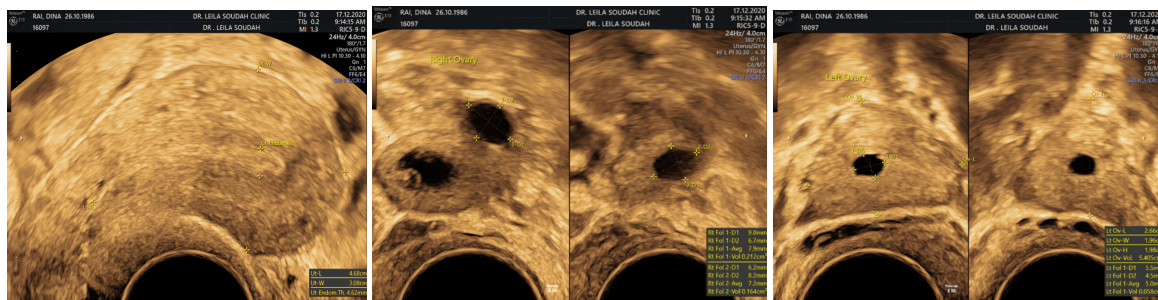


Fig. 1. 1st Gynae ultrasound; 2nd cycle day

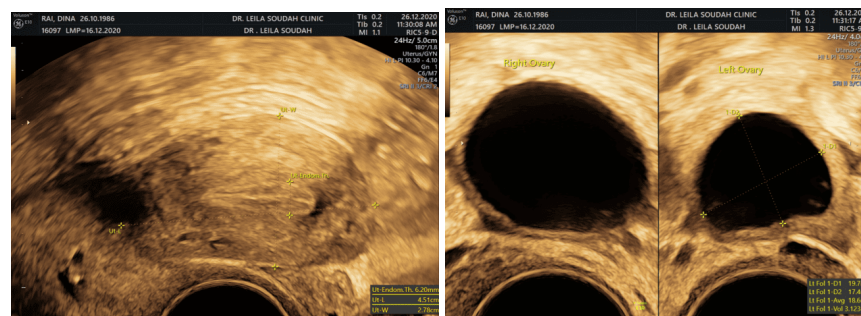


Fig. 2. 2nd Gyne ultrasound; 11th cycle day

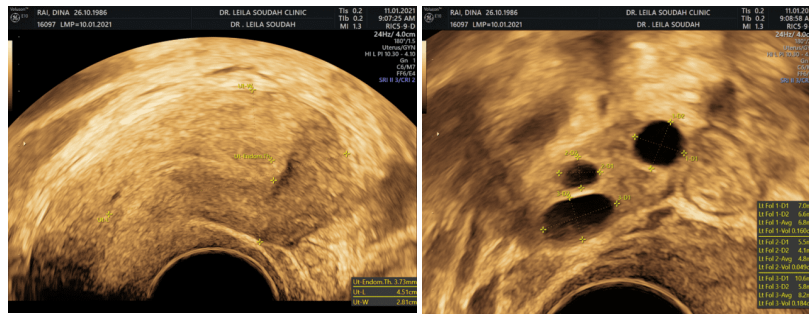
Table 1
Prescribed Supplements and doses for treatment

Supplements	Dosage	Frequency
NAC	750mg	1 Cap 3 Times a day for 90 days
OPC Formula		1 Capsule Twice a day for 90 days
Orthomol Natale		Once daily for 90 days (will be taken after food)
Omega 3 EPA/DHA 3/2	950 mg	1 tabs twice daily for 90 days
Probiotic (Omni Lactis)		1 Cap 3 Times daily for 90 days
Tab Vitamin D	2000 I.U	3 Tab daily for 2 Months, then Recheck the Level (to be taken at night)
Polysitol	600 mg	1 Tab daily night for 30 days
Tab Zinc	25 mg	1 tab once a day for 60 days (to be taken in the morning)
Tab Chelated Copper		1 tab Once a day for 60 days (to be taken in the night)
Cap Saw Palmetto	160mg	1 Cap once a day for 30 days
Tab Aspirin	75 mg	1 Tab once a day for 30 days
Tab Vitamin B6 Activator Active Form		1 Tab Once a day for 60 day
Cap Vitamin B12	500 mcg	1 Cap once a day for 60 days
Tab Melatonin Sublingual	0.25 mg	1 Tab once a day for 30 days (to be taken at night)

dosage can increase egg quality, but not egg number and embryo quality [36]. Our case study, indicates quality over quantity. We only obtained two follicles, one egg, and one frozen embryo. For the second treatment cycle, we took GH, 4 IU Clomid 150 mg, and GF 150 IU and started two cycle days. On her 7th cycle day, there were improvements. We increased GF from 150 to 225 units to encourage the growth of small follicles. Ultrasound was performed as shown in figure 4. Two mature Follicles were observed, two eggs were collected, fertilized, and two embryos were produced. Only one embryo developed. The other was of poor quality.

However, her melatonin levels were not measured, and we opted to provide a modest dosage of bioidentical melatonin SL IR 0.25. Melatonin enhances egg quality, leading to a 30% rise in fertility (Espino et al., 2019). Research indicates that melatonin supplementation in the culture media increases the rate of day three embryos [37].

On her 3rd treatment cycle, following the second day, an ultrasound was performed, as shown in figure 3. A Cyst was observed at 27/14 mm on the right side; the left side was silent. We gave her a one-month course of Yasmeen to remove the cyst. The patient's Estradiol levels had increased to 242.71



pg/mL, as shown in Table 3. The presence of the cyst was cross checked by ultrasound (figure 5 and 6). So the third cycle was skipped.

At the fourth treatment cycle, 1/03/21, following her second day, the protocol was prepared for embryo transfer. One experienced physician in the fertility centre suggested a plan and explained it to the patient, ensuring she understood everything. It was recommended that Decapeptyl would be administered to the patient on days 2 and 3 of the cycle. There was no dose for the fourth and fifth cycles, but TDS estradiol was introduced on days 6-12 of the cycle. Meanwhile, infection test HVS and Mycoplasma were recorded as negative.

At the seventh appointment, on the 12th day of the cycle, a repeat ultrasound (figure 7) and a blood test was performed for the embryo transfer. The patient was on Estrogen 2mg TDS, whereas the estradiol was 686.56 pg/mL. The patient was prepared to undergo embryo transfer. Almost two weeks later, on 25/3/2021, BHCG and progesterone were done, showing early pregnancy (Figure 8).

3. Discussion

In recent years, AMH has emerged as a critical component in

the assessment of amenorrhoea. Recent research has demonstrated a significant association between AMH levels and pregnancy rates [38, 39]. The pregnancy rate is predicted to be lower when the AMH level is low [40, 41]. However, the prognosis for women with extremely low AMH levels (0.5 ng/ml) who undergo IVF is significantly influenced by chronological age. Although a high risk of cycle cancellation is associated with very low AMH levels, it should not exclude a couple from IVF treatment [42]. In our case, the patient had low levels of AMH, but following a holistic approach, she could conceive. We suggested that patient about adopting a healthy lifestyle and advised the couple to quit smoking and drinking. Also, avoid consuming milk and milk products. The patient strictly followed vitamins and mineral-rich supplements.

On 25/03/21, the patient was pregnant. A pregnancy test per blood positive was recorded (BHCG level 103.17 mIU/mL indicated signs of early pregnancy). On 14/4/2021, pregnancy seen intrauterine with fetal heart-positive FH levels were elevated. After consulting with an IVF specialist, the patient was administered proglyton 2 tablets for eight weeks. One pill for 10 weeks, then discontinued. The patient was advised to administer Progesterone vaginally. The patient was also

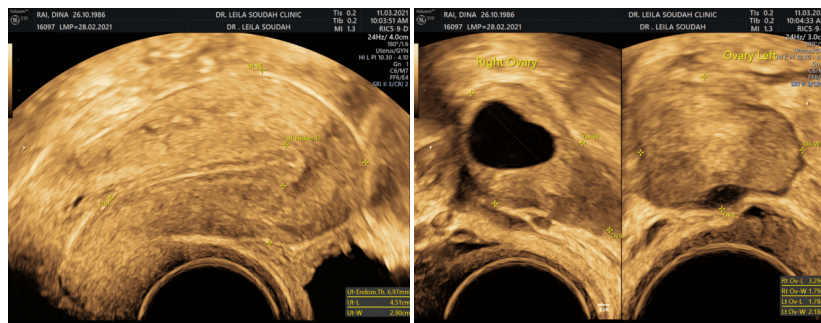


Fig. 7. 7th visit Gynae ultrasound; 12th cycle day

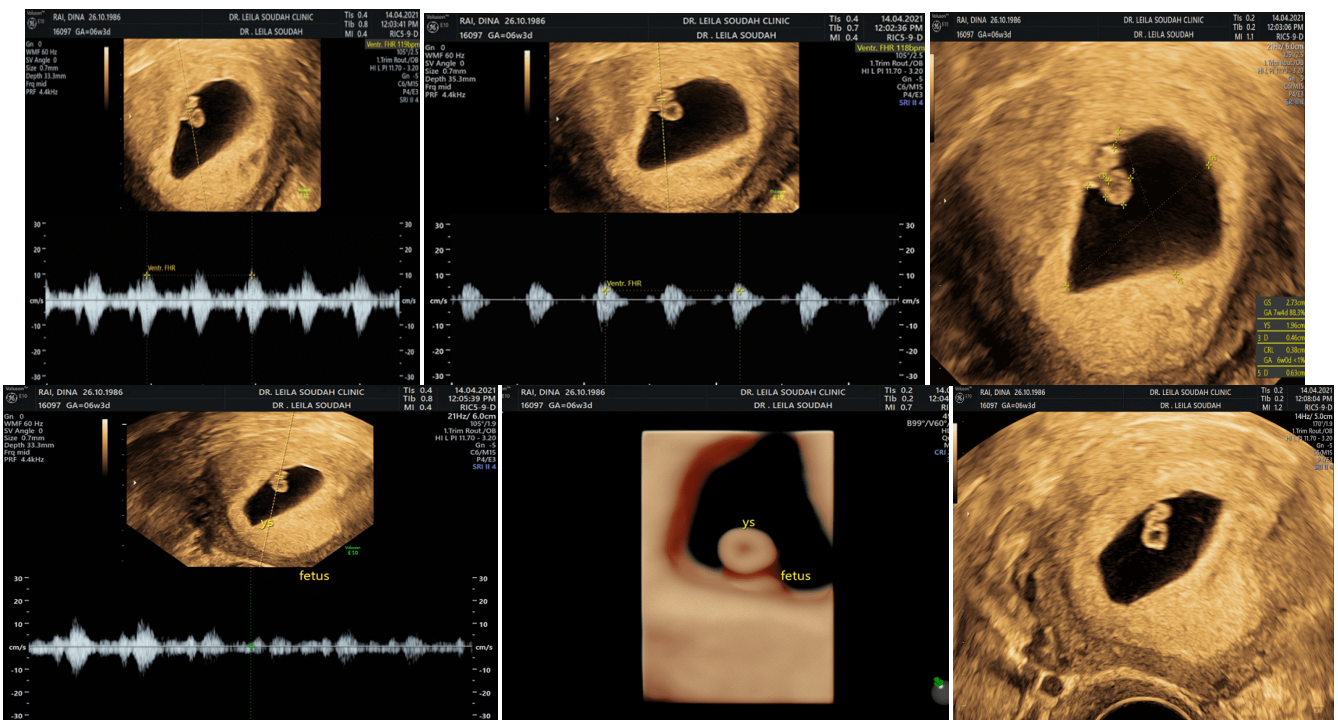


Fig. 8. 8th Gynae ultrasound; 6+5 weeks of pregnancy

advised to take aspirin, prednisolone, and Alaract. Alaract was prescribed only after the patient's 14 weeks of pregnancy as it will control her sugar and insulin levels and reduce inflammation and chances for premature delivery. Follow-ups are reported in appendix A. In April 2021, she returned home with a healthy baby. Melatonin is an important hormone generated by the pineal gland's posterior lobe [43]. According to a study, melatonin levels may help with infertility and pregnancy, including recurrent miscarriages [44]. This hormone is produced throughout the night [15]. Maximum levels of melatonin range from 12 to 2, and the brain must begin producing it around one hour after falling asleep. After a change in sleep routine, the menstrual cycle of a patient who works night shifts or often travels to a foreign continent will begin to alter [45, 46]. Recent research has indicated that oral melatonin administration lowers intrafollicular cell stress and boosts fertilisation rates [27]. Melatonin may improve the quality of poor-quality eggs and defrosted embryos [37].

Table 2

Initial laboratory values for 1st, 2nd and 3rd Gynae Ultrasound Visits

Laboratory Test	Result
Fasting Insulin	6.69 uIU/mL
Fasting Blood Sugar	90.42 mg/dL
Homa Index	1.49
Homocystein	9.00 umol/L
Ferritin	29.01 ng/mL
Vitamin D	26.10 ng/mL
Zinc	12.00 umol/L
HORMONES (2nd cycle day)- 1st VISIT	
Testosterone	0.52 ng/mL
FSH	14.22 mIU/mL
LH	3.61 mIU/mL
Estradiol	39.72 pg/mL
Prolactin	18.07 ng/mL
DHEA	10.98 umol/L
Bioavailable testosterone	12.8 ng/dL
Anti-Muller Hormone	0.11 ng/mL
LFT, RFT, CBC	✓
HIV, HCV, TPHA, HbsAg	Negative
Blood Group & RH	"B" Positive
Indirect Coomb's Test	Negative
Mycoplasma	Ureaplasma Positive
MSU	No Growth After 48 Hours
COAGULATION PROFILE	
Prothrombin Time	12.2 ✓
INR	1.05 ✓
APTT	31.80 ✓
HORMONES (11th cycle day)- 2nd VISIT	
FSH	11.26 mIU/mL
LH	11.43 mIU/mL
Estradiol	1066.75 pg/mL
Progesterone	1.10 ng/mL
HORMONES (2nd cycle day)-3rd VISIT	
FSH	6.79mIU/mL ✓
Estradiol	41.35pg/mL ✓

Table 3

Laboratory values for 4th & 5th Gynae Ultrasound Visits

Laboratory Test	Results
HORMONES (7th cycle day)- 4th VISIT	
LH	7.63 mIU/mL (Decreasing)
Estradiol	342.77 pg/mL (Increasing)
HORMONES (10th cycle day)- 4th VISIT	
LH	6.59 mIU/mL ✓
Estradiol	1007.50 pg/mL ↑
HORMONES (2nd cycle day)- 5th VISIT	
Estradiol	242.71 pg/mL ↑
INFECTION TEST	
HVS	Negative
Mycoplasma	Negative

Table 4

Laboratory value for hormones before and after embryo transfer

HORMONES	
B-HCG	103.17 mIU/mL
Progesterone	22.73 ng/mL (Slightly low for 1st trimester)
<i>BHCG level indicates signs of early pregnancy.</i>	

Test	Result
HORMONES (12th cycle day)-7th VISIT	
LH	6.85 mIU/mL ✓
Estradiol	686.56 pg/mL ↑
Progesterone	0.74 ng/mL ✓
<i>Patient is ready for embryo transfer</i>	
<i>Patient is on Estrogen 2mg TDS</i>	
AFTER 3 MONTHS OF EMBRYO TRANSFER	

4. Conclusion

This paper presented a case study to increase female fertility with very low AMH.

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