Original Article

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# Trends in Anti-Mullerian Hormone levels among Women attending Fertility Clinic in the UAE.

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## ABSTRACT

**Background:** Anti-Müllerian hormone (AMH) is widely recognised as the gold standard for assessing ovarian reserve. It is also utilised to predict ovarian response during controlled ovarian stimulation in assisted reproductive technology (ART) and is key indicator of oocyte yield, embryo quality, embryo euploidy, and live birth rates.
**Methods:** This multicentre retrospective study analysed the prevalence of AMH levels in women aged 18–50 years who attended Fakih IVF Fertility Centres (Abu Dhabi, Al Ain, and Dubai) in the UAE for their initial fertility consultation between 2017 and 2023. AMH levels were classified as normal (≥1.3 ng/mL) or low (<1.3 ng/mL).
**Results:** A total of 8,533 women underwent AMH testing, with 63.62% having normal AMH levels and 36.38% showing low AMH levels. No significant differences in AMH levels were observed across demographic groups. From 2017 to 2021, normal AMH levels remained stable at around 63-65%, but in 2022-2023, they declined to 58-59%, indicating a 5-7% increase in the number of patients with low AMH. This rise was particularly notable, with a 4.3-8.3% increase in women under 30 and a 7.7-9.5% increase in those aged 31-40.
**Conclusion:** This study reveals a decline in AMH levels across all age groups during 2022-2023 compared to the previous five years, with a more significant decrease noted in women under 40. Given AMH's role as a key predictor of successful ART outcomes, early intervention for women under 40 years particularly those under 35, may be crucial for improving ART success. Further research with a larger sample size is necessary to confirm these findings.

**Keywords :** Anti-Mullerian Hormone, Ovarian reserve, assisted reproductive technology, Age, year.

## BACKGROUND

Anti-Mullerian Hormone (AMH) is a dimeric glycoprotein belonging to the transforming growth factor-beta (TGF-β) superfamily, particularly the TGF-β group [1]. AMH shares structural similarities with other TGF-β ligands such as inhibin and activin. In females, AMH primarily functions in the regulation of folliculogenesis and growth control [2]. It is secreted by granulosa cells surrounding growing ovarian follicles, with expression beginning in the primary follicles and increasing from the secondary stage until the small antral follicle stage [3]. In humans, this occurs when ovarian follicles reach a diameter of 4–6 mm [4]. The oocyte is enclosed by somatic support cells, which develop within the ovarian follicle [5]. As the oocyte matures, these somatic cells undergo division and specialization, producing steroid hormones. Folliculogenesis is a complex physiological process involving the release of a mature oocyte and its subsequent transformation into a corpus luteum [5].
AMH levels increase from birth and stabilize around the age of 25, following a significant rise during adolescence, particularly until around age 16. This increase is thought to correspond with the activation of primordial follicles between infancy and age 14 [3]. After age 25, AMH levels gradually decline until they become undetectable at the onset of menopause. However, variations in AMH levels may occur due to ethnic differences [3].

Serum AMH is widely regarded as the gold standard for evaluating ovarian reserve [6]. The Roche enzymatic immunoassay is commonly used to measure AMH levels in the blood, providing critical insights into ovarian reserve [7,8,9] According to the American Society for Reproductive Medicine, ovarian reserve refers to the number of oocytes remaining in the ovaries throughout a woman's life cycle [10,11]. AMH levels serve as a reliable estimate of the remaining oocyte pool and the primordial follicle reserve [12]. In females, AMH is produced by granulosa cells during the reproductive years and declines with age as ovarian reserve diminishes [13]. The measurement of serum AMH is crucial in fertility evaluation and treatment planning, providing an indication of follicle count and ovarian function [14,15].In addition to AMH, other biomarkers, such as early follicular-phase FSH, LH, estradiol, inhibin B, and transvaginal ultrasonography for antral follicle count (AFC), are used to assess reproductive potential and fertility, often in conjunction with patient age [16,17].

Serum AMH is a predictive biomarker for controlled ovarian stimulation in assisted reproductive technology (ART) through the administration of exogenous gonadotropins [18]. It provides prognostic information for ART, including ovarian stimulation response, oocyte quality, embryo quality, and fertility outcomes [6]. AMH testing is routinely used in the diagnosis and treatment of women experiencing infertility, including conditions such as polycystic ovary syndrome (PCOS), ovarian hyperstimulation syndrome (OHSS), menopause prediction, and monitoring the effects of chemotherapy and radiation on ovarian function [19]. Women diagnosed with PCOS typically exhibit elevated AMH concentrations [20].

Recent research has identified the presence of AMH and its receptor AMHR2 in several extragonadal tissues, including the uterus, placenta, lungs, mammary glands, hypothalamus, pituitary gland, motor neurons, and both central and peripheral nervous systems [21]. This highlights the diverse physiological roles of AMH beyond the ovaries, suggesting non-reproductive functions [21]. Additionally, AMH serves as a key tumour biomarker for assessing treatment response and monitoring recurrence in ovarian malignancies, such as granulosa cell tumours [6]. It also has potential as a prognostic marker for ovarian reserve preservation following cancer treatment, making it relevant in onco-fertility [19].

Environmental factors and genetic predispositions have been shown to influence AMH levels [22]. While aging decreases oocyte production in the ovaries, conditions such as PCOS can lead to elevated AMH levels [23]. AMH level fluctuations do not typically present with symptoms, but changes in AMH may indicate underlying reproductive health issues [13]. Elevated AMH levels may indicate increased ovarian reserve but could also be linked to ovulatory dysfunction, which could affect fertility [24,25]. Conversely, low AMH levels are associated with irregular menstrual cycles, fertility challenges, reduced ovarian reserve, and the potential onset of menopause [24,26]. Ovarian reserve assessments include both biochemical tests like AMH and pelvic ultrasound to evaluate ovarian volume and antral follicle count [27].

Thus, this study aimed to evaluate prevalence of AMH levels over a seven-year period among women aged 18 to 50 years attending fertility clinics. The study also sought to determine if AMH levels and ovarian reserve remained consistent over the same period.

## METHODOLOGY

A retrospective study was conducted to analyse the prevalence of Anti-Müllerian Hormone (AMH) levels among women over the years in the UAE. The study included 8,533 women aged 18 to 50 years who attended fertility clinics for their first consultation and underwent ovarian reserve testing with AMH. These women were seen at Fakih IVF fertility centres (Abu Dhabi, Al Ain, Dubai) in the UAE from 2017 to 2023.

The primary focus of the study was to examine the distribution of normal and low AMH values over time, differentiated by year and age group. Key variables included AMH levels (normal or low), age categories, and year. Proportions of individuals with normal and low AMH levels were calculated within each year and across different age groups.

AMH levels were classified as normal (≥1.3 ng/mL) or low (<1.3 ng/mL). Serum AMH quantification was conductedat Unilab Clinical Laboratory using a fully automated Elecsys® assay (Roche) in accordance with the manufacturer's instructions. The assay had a measuring range from 0.01 to 23 ng/mL, with a test imprecision of less than 5%.

Data were extracted from electronic health records (Meditex, Germany) and entered into an Excel spreadsheet to summarize the distribution of AMH levels in the UAE population. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 20.0 (SPSS Inc., Chicago, IL, USA). Subgroup analyses were conducted based on age and ethnicity.

## RESULTS

A total of 8,533 women underwent AMH testing during their first visit to Fakih IVF Fertility Centres between 2017 and 2023, with an annual average of 1,219 ± 113 patients. Of these, 776 ± 81 women (63.62%) had normal AMH levels, while 443 ± 58 women (36.38%) had low AMH levels. No significant differences were observed in AMH results across various demographic groups.

Analysis of AMH levels over time revealed that the proportion of women with normal AMH remained relatively the same at approximately 63-65% between 2017 and 2021. However, a decline was noted in 2022-2023, with normal AMH levels

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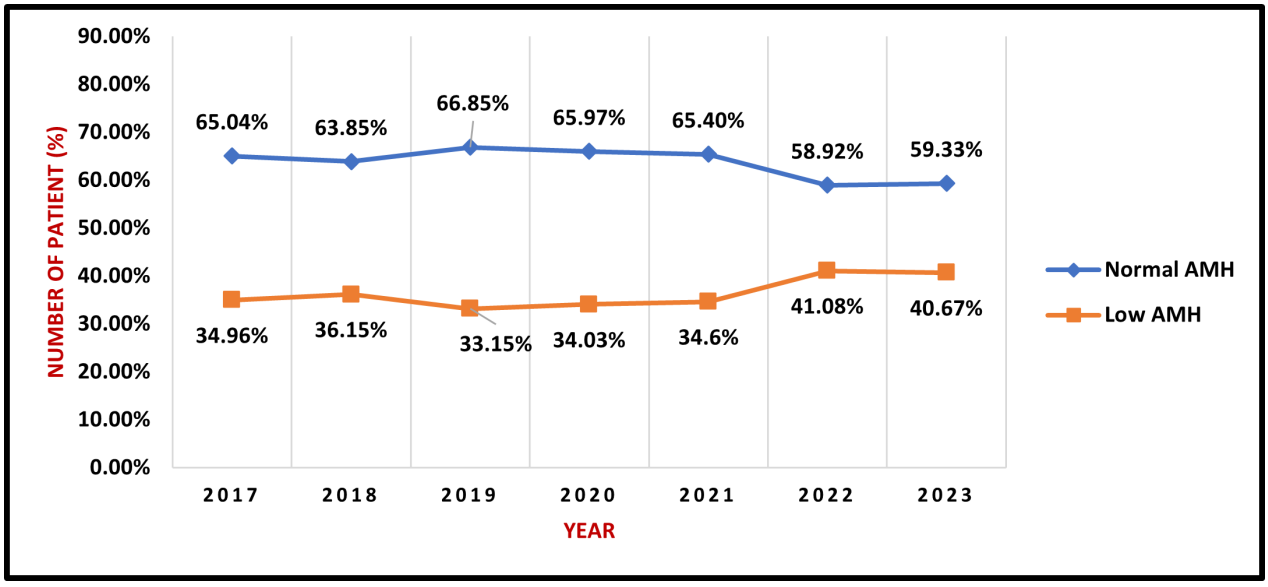
decreasing to 58-59%. Consequently, the proportion of women with low AMH, which was around 33-36% from 2017 to 2021, increased to 40-41% in 2022-2023. This represents a 5-7% decrease in normal AMH levels and a corresponding 5-7% increase in low AMH levels, as shown in **Table 1** and **Figure 1**.

**Table 1.** Year wise distribution of Normal AMH and Low AMH levels.

| Year | Normal AMH | | Low AMH | | Total Population |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 2017 | 774 | 65.04% | 416 | 34.96% | 1190 |
| 2018 | 779 | 63.85% | 441 | 36.15% | 1220 |
| 2019 | 831 | 66.85% | 412 | 33.15% | 1243 |
| 2020 | 787 | 65.97% | 406 | 34.03% | 1193 |
| 2021 | 843 | 65.40% | 446 | 34.60% | 1289 |
| 2022 | 816 | 58.92% | 569 | 41.08% | 1385 |
| 2023 | 601 | 59.33% | 412 | 40.67% | 1013 |

**Figure 1.** Year wise distribution of Normal AMH and Low AMH levels




The cohort of 8,533 women was subdivided by age: 21.55% were under 30 years old (n = 1,839), 49.63% were between 31 and 40 years old (n = 4,235), and 28.81% were between 41 and 50 years old (n = 2,459), as shown in **Table 2** and **Figure 2**.

**Table 2.** Age wise distribution of Normal AMH and Low AMH.

| Age | Normal AMH | | Low AMH | | Total Population |
|---|---|---|---|---|---|
| | n | % | n | % | |
| <30 | 1558 | 84.7% | 281 | 15.3% | 1839 |
| 31-40 | 2649 | 62.6% | 1586 | 37.4% | 4235 |
| 41-50 | 1224 | 49.8% | 1235 | 50.2% | 2459 |

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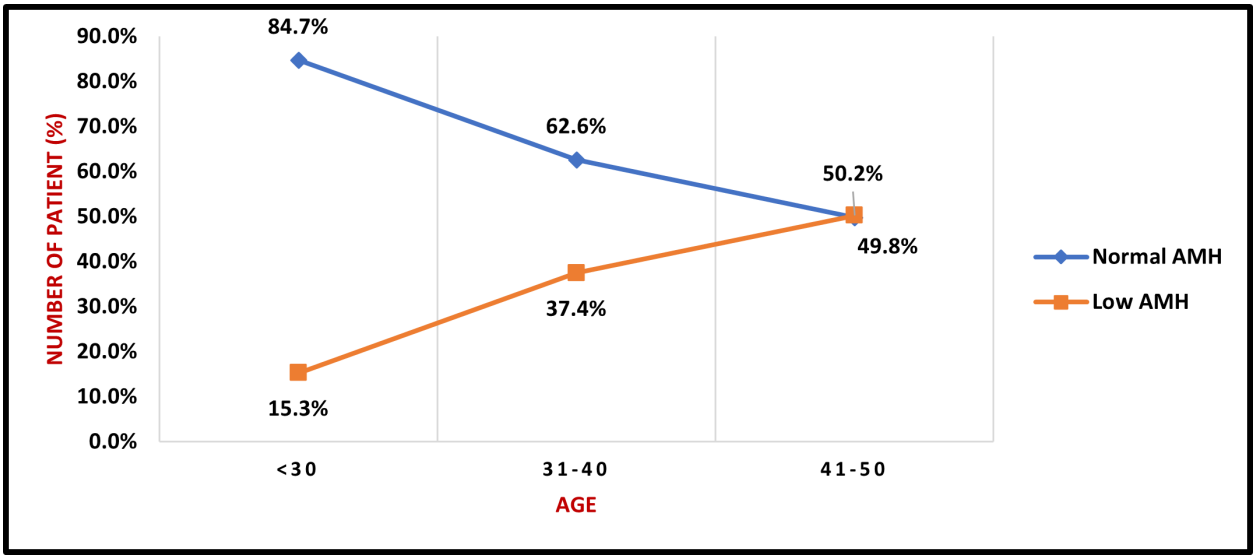
**Figure 2.** Age wise distribution of Normal AMH and Low AMH.

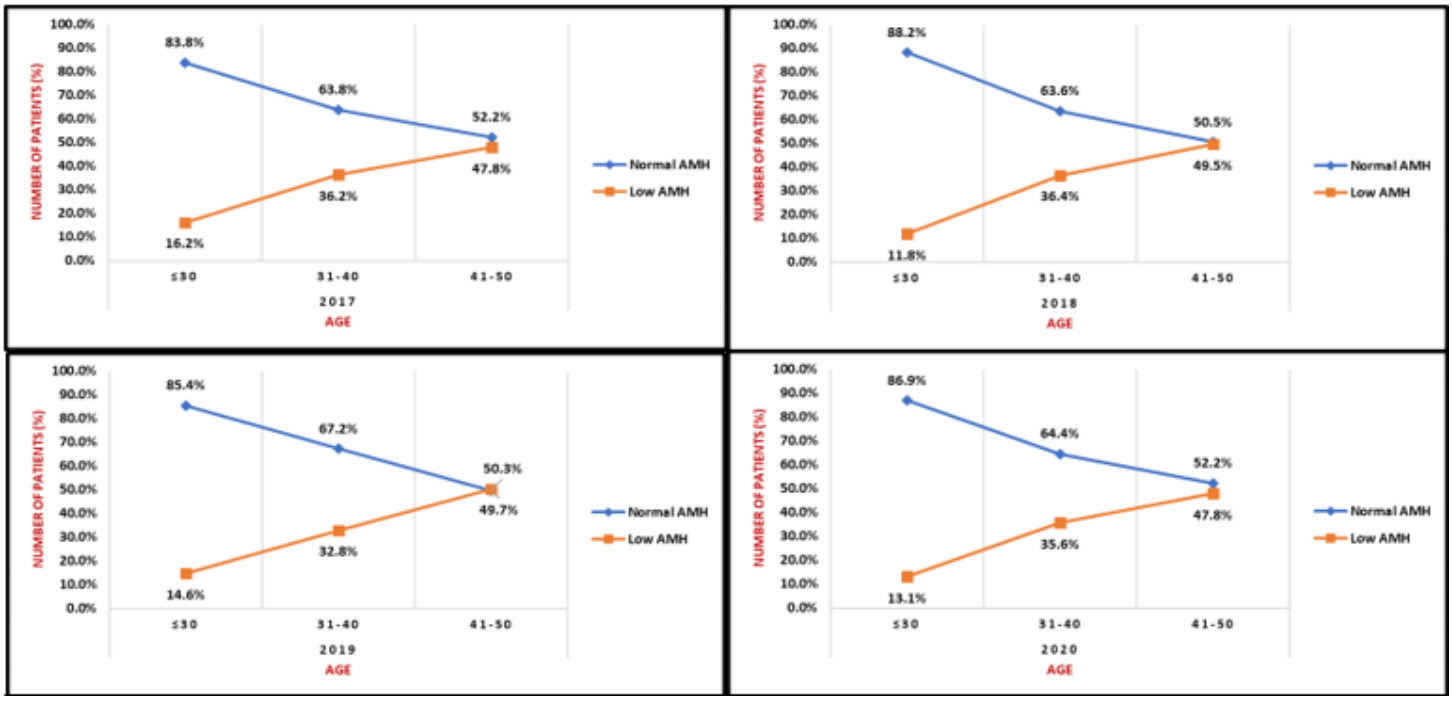



Among women under 30 years of age, 84.7% had normal AMH levels, while 15.3% had low AMH. The percentage of women in this age group with normal AMH levels ranged from 83.8% to 89.1% between 2017 and 2021, but this percentage declined by 4.3-8.3% to 79.5-80.8% in 2022-2023. Correspondingly, the proportion of women with low AMH increased from 10.9-16.2% in 2017-2021 to 19.2-20.5% in 2022-2023, representing an increase of 4.3-8.3% as shown in figure 3.

In the 31-40 age group, 62.6% of women had normal AMH levels, while 37.4% had low AMH. Between 2017 and 2021, 63.8-66% of women in this age group had normal AMH levels, but this declined by 7.7-9.5% to 54.3-58.3% in 2022-2023. Similarly, the proportion of women with low AMH increased from 34-36.2% in 2017-2021 to 41.7-45.7% in 2022-2023, reflecting a 7.7-9.5% increase as shown in figure 3.

Among women aged 41-50 years, 49.8% had normal AMH levels, while 50.2% had low AMH. From 2017 to 2021, the proportion of women with normal AMH levels ranged from 48.7% to 52.2%, but this percentage declined by 0.6-4.8% to 47.4-48.1% in 2022-2023. In parallel, the proportion of women with low AMH increased from 47.8-51.3% in 2017-2021 to 51.9-52.6% in 2022-2023, an increase of 0.6-4.8% as shown in **figure 3**.

**Figure 3.** Year and Age wise distribution of Normal AMH and Low AMH levels



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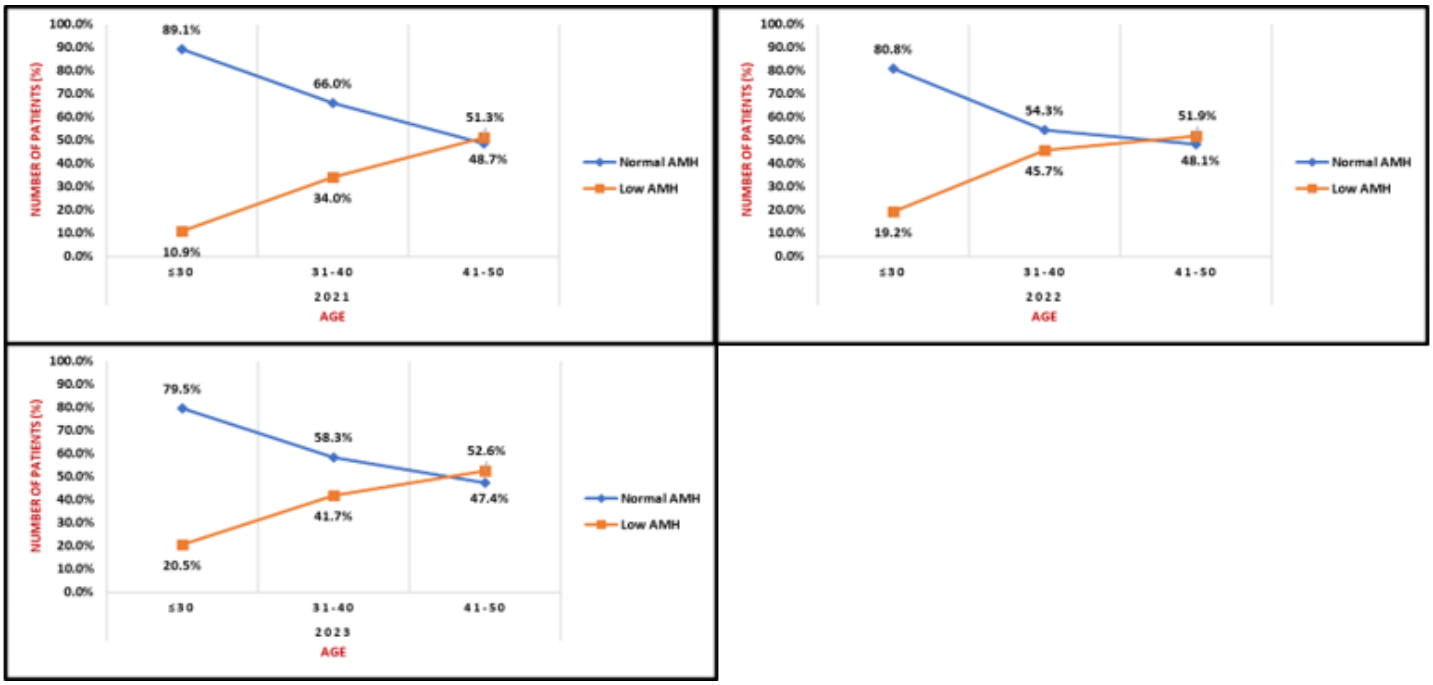


## DISCUSSION

Anti-Müllerian hormone (AMH), produced by granulosa cells in developing ovarian follicles, serves as an indicator of the number of growing follicles [28]. Serum AMH levels have emerged as a well-established marker of ovarian reserve [3]. In adult women, there is a strong inverse correlation between AMH levels and age, making AMH a valuable tool for assessing follicle development, comparable to other markers of ovarian function such as FSH, estradiol, and inhibin B [29]. Serum AMH levels exhibit minimal intra-cycle fluctuation, making them useful in predicting fertility and the likelihood of natural conception [28,30]. AMH is commonly measured as a baseline indicator of ovarian reserve prior to the initiation of assisted reproductive technologies (ART) to assess ovarian response to gonadotropins [31] and to predict the prognosis of in vitro fertilization (IVF) cycles [32]. AMH levels allow for tailored controlled ovarian hyperstimulation (COH), facilitating the prediction of ovarian response to gonadotropins [33,34,35]. AMH has also been linked to oocyte survival rates after vitrification, as well as embryo quality, euploidy, and miscarriage rates [36]. Lower AMH levels are associated with poor pregnancy outcomes in women undergoing infertility treatment and reduced ovarian responsiveness to gonadotropin stimulation [37].

Various studies previously have validated AMH as a reliable predictor of ovarian responsiveness [38,39,40], making it a crucial marker for anticipating ovarian response to controlled ovarian hyperstimulation (COH). A meta-analysis of nine trials involving 1,500 patients demonstrated that AMH is a valid marker for predicting an overactive ovarian response [40,41]. Lee et al 2008 suggested that AMH was a more reliable predictor than other factors such as age, body mass index (BMI), baseline FSH, or inhibin B [39]. AMH levels were strongly correlated with antral follicle count (AFC), the number of follicles observed via ultrasound, the number of oocytes retrieved, the maturation stage of oocytes, and the number of frozen embryos. Therefore, AMH is a dependable biomarker for predicting women's response to fertility treatments [40].

An earlier study identified a negative correlation between AMH levels and patient age, with median AMH levels decreasing from 6.71 (2.91) ng/mL in younger patients to 0.68 (0.45) ng/mL in women over the age of 50. The median AMH levels declined by an average of 0.12 ng/mL per year after the age of 35, compared to a previous decline of 0.27 ng/mL per year [37]. Consistent with previous studies, age was inversely correlated with circulating AMH levels in adult females [42].

An earlier study in the region found that women with diminished ovarian reserve, defined as AMH levels below 1.3 ng/mL, had a lower probability of obtaining at least one blastocyst biopsy and a lower chance of producing a euploid blastocyst per ovarian stimulation cycle [43]. Additionally, 40.60% of women in the MENA (Middle East and North Africa) region were found to have AMH levels below 1.3 ng/mL [44]. Our study results differ slightly from the previous study in the same region as our findings suggest that 36.3% of women presenting to fertility clinics in the UAE had AMH levels below 1.3 ng/mL, indicating diminished ovarian reserve. The decline in AMH levels is more in last couple of years compared to previous years. More importantly, no significant differences were observed in AMH levels across different demographic groups.

In a recent study, Chinese women were shown to experience a decline in AMH levels with age, with a 28% and 80%

reduction at ages 30 and 45, respectively [45]. Moreover, Chinese women exhibited higher peak AMH levels at age 25 compared to European women [46]. In contrast, African and American women were observed to have lower serum AMH levels compared to White women [47].

Emerging evidence suggests that ovarian reserve is influenced by various factors, including sociocultural environment, lifestyle, and ethnicity [40]. Studies have shown that women of Asian, African, American, Hispanic, and Indian backgrounds have lower live birth rates and higher miscarriage rates following ART compared to their White or Caucasian counterparts [48,49,50].

## CONCLUSION

This study highlights a decline in AMH levels among women attending Fakih IVF fertility clinic from 2022-2023, impacting all age groups compared to the previous five years. The decrease was particularly notable in women under 40, though no significant differences in AMH levels were observed across various demographic factors. Further research with a larger sample size is needed to validate these findings.

Given the role of AMH as a biomarker of ovarian reserve and its significance in predicting successful assisted reproductive technology (ART) outcomes, early intervention for women under 40 years particularly those under 35 years old may be crucial for improving ART success.

Regular monitoring of AMH levels in fertility clinics on a yearly basis is essential to gain a deeper understanding of its trends and implications for reproductive health in the UAE.

### Ethics Approval and Consent to Participate

This study was conducted in full compliance with ethical standards and guidelines. The research protocol and data collection procedures were approved by the Internal Research Ethics Committee of the First IVF Fertility Centre (Committee REC - FIVF-012) and the Abu Dhabi Health Research and Technology Committee (Approval No. DOH/CVDC/2023/1997). All necessary measures were taken to ensure the confidentiality and privacy of participants' personal information throughout the study.

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### Declaration of Interest

The authors declare no conflicts of interest and have no affiliations or financial involvements with any organization or entity with a financial interest in the subject matter discussed in this manuscript. This includes employment, consultancies, honoraria, expert testimony, grants, or royalties.

### Funding

No funding was received for this study.

### Data Availability Statement

The data supporting the findings of this study are stored in the Meditex software, which is specifically designed for In-Vitro Fertilization (IVF) clinics. Meditex is used to manage and document patient data within assisted reproduction organizations. However, due to licensing agreements associated with this study, access to the data is restricted. The authors are open to providing access to the data upon reasonable request.

### Author Contributions

All authors contributed equally to this manuscript.

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