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Original Research Article

Comparison of control oocytes and oocyte with mild and dark severe coarse granules in the perivitelline space: insights on IVF-ICSI cycle outcomes: a retrospective cohort analysis

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ABSTRACT

Background: Coarse granules in the perivitelline space (PVS) have been associated with impaired oocyte quality and reduced success rates in assisted reproductive technologies. However, their precise impact on IVF-ICSI cycle outcomes remains unclear. This study aims to evaluate the correlation between PVS granularity and embryological as well as clinical outcomes.

Methods: This retrospective cohort study analyzed 161 women undergoing IVF/ICSI cycles at Nova IVF Fertility Centre, Madurai, between January 2022 and March 2025. Oocytes (n=2300) were classified into three groups based on the presence of PVS granules: Group A (Control oocytes), Group B (Moderate granules), and Group C (Dark severe granules). Statistical analyses assessed differences in oocyte maturation, fertilization, embryo development, implantation, and live birth rates.

Results: Group C exhibited significantly higher AMH levels ($p<0.008$) and increased oocyte retrieval rates ($p<0.039$). However, fertilization efficiency, cleavage rates, and implantation rates were significantly lower in both Group B and Group C. ROC analysis identified MII oocytes (AUC=0.683) and fertilization rates (AUC=0.674) as the strongest predictors of implantation success. The clinical pregnancy rate was highest in Group A (79.3%) and lowest in Group C (40.2%) ($p<0.000$). Despite a comparable live birth rate between Groups A and C, ongoing pregnancy rates were significantly lower in Group C (13.4%).

Conclusions: Dark severe granules in PVS negatively impacts oocyte competence and IVF success. Optimizing ovarian stimulation protocols and incorporating advanced embryo selection techniques may improve ART outcomes for patients with granular oocytes.

Keywords: AMH, Assisted reproductive technology, Embryo development, IVF-ICSI, Oocyte granularity, Perivitelline space, Pregnancy outcomes

INTRODUCTION

Evaluation of oocyte quality is a crucial factor in determining the efficacy of assisted reproductive technology (ART), especially in intracytoplasmic sperm injection (ICSI) and in vitro fertilization (IVF) cycles. Oocyte morphological anomalies, such as cytoplasmic and perivitelline space (PVS) irregularities, have been thoroughly investigated for their possible effects on implantation success, embryo development, and fertilization. Among these, the presence of coarse granules in the PVS has emerged as a key morphological feature associated with compromised embryological outcomes, yet its precise implications remain inadequately defined.[1]

According to recent research, the PVS's coarse granules may indicate underlying cytoplasmic immaturity, which may be caused by either excessive gonadotropin stimulation or inadequate folliculogenesis.[2] These cytoplasmic changes have been connected to abnormal zona pellucida structure, mitochondrial malfunction, and elevated oxidative stress, all of which can have detrimental effects on early embryonic development and fertilization rates.[3] Therefore, it is crucial to assess the importance of PVS granularity in forecasting ART outcomes to improve stimulation protocols and oocyte selection criteria.

A higher frequency of oocytes with coarse granules has been commonly linked to polycystic ovary syndrome (PCOS), mainly because of disturbed follicular maturation and a changed hormonal environment.[4] Since PCOS patients frequently exhibit high levels of anti-Müllerian hormone (AMH) and increased follicular recruitment, PVS granularity in this group may indicate a cytoplasmic maturation defect rather than an ovarian hyperstimulation-related issue.[5,6] Understanding the pathophysiological mechanisms underlying these morphological alterations is crucial for devising individualized treatment strategies to enhance ART success rates.

This study aims to provide a comprehensive evaluation of the impact of PVS granularity on IVF-ICSI cycle outcomes by analyzing fertilization rates, embryo quality, implantation success, and clinical pregnancy rates across different degrees of granules present in PVS. By elucidating the clinical relevance of this morphological feature, our findings will contribute to the ongoing efforts to optimize ART protocols and improve patient-specific reproductive outcomes.

METHODS

This retrospective cohort study was conducted at Nova IVF Fertility Centre, Madurai, Tamil Nadu, India, from January 2022 to March 2025. The study involved 161 women undergoing IVF/ICSI cycles due to various infertility factors. A total of 2300 oocytes were retrieved and classified into three groups based on the presence of coarse granules in the PVS: Group A (Control oocytes, n=870), Group B (moderate coarse granules, n=830), and Group C (dark severe coarse granules, n=600) (Figure 1). Oocyte retrieval was performed using standard transvaginal aspiration protocols. Key outcomes included maturation (MII oocytes), fertilization, cleavage, embryo quality assessment, implantation rates, and live birth outcomes.

Inclusion criteria

This retrospective study included couples who met the following criteria: male partners with normozoospermia as defined by WHO 2010 guidelines; female partners aged between 25 and 35 years; male partners aged between 25 and 40 years; and all cases involving ICSI with embryos cultured to the blastocyst stage (Day 5 or Day 6).

Exclusion criteria

Cases were excluded if there was evidence of male factor infertility, including oligoasthenoteratozoospermia (OAT), teratozoospermia (TZ), or Y-chromosome microdeletions involving the TDF1 gene. Additional exclusion criteria included female age greater than 35 years, male age greater than 40 years, and the use of conventional IVF rather than ICSI.

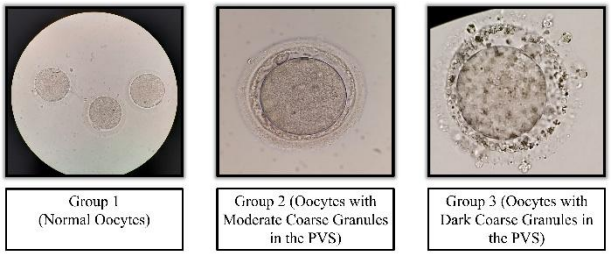

Figure 1: Classification of the oocytes.

Statistical analysis

Demographic, clinical, and embryological data were systematically collected and analyzed. Statistical analysis was performed using IBM SPSS Software v26.0. Continuous variables were compared using independent sample t-tests, while categorical variables were analyzed using chi-square tests. Receiver Operating Characteristic (ROC) analysis was applied to evaluate the predictive ability of embryo quality for implantation success, with an area under the curve AUC>0.75 considered significant. Results were interpreted to assess the impact of granules in PVS on embryological and clinical outcomes.

RESULTS

Table 1 presents the demographic information of the respondents, comparing three groups based on the presence of coarse granules in the perivitelline space. The mean age, BMI, infertility duration, and infertility type (primary or secondary) were similar across the three groups, with no significant differences ($p>0.05$). However, the AMH levels showed a significant difference, with Group C (dark severe coarse granules) having the highest mean AMH (5.7±4.1), compared to Groups A (3.3±2.6) and B (3.7±2.9), with a p value of 0.008. Regarding infertility factors, there was a significant difference between the groups ($p<0.000$). Group C had the highest proportion of women with polycystic ovaries (PCO) (45.1%), followed by Group B (31.6%), while Group A had a relatively lower percentage (23.0%). The presence of other infertility factors, such as tubal factor, low reserve, and hypothyroidism, varied between the groups, with Group C having the highest prevalence of low ovarian reserve (19.5%) and PCO, while Group A had a higher proportion of women with low ovarian reserve.

Table 2 presents the clinical and morphological characteristics of the respondents, comparing the three

groups based on the presence of coarse granules in the perivitelline space. There were no significant differences between the groups in the number of follicles, sperm quality, number of embryo transfers (ET), or embryo vitrification (p>0.05). However, several key clinical factors showed significant differences. Group C (dark severe coarse granules) had significantly higher levels of FSH (238.1±33.6) and HMG (137.9±91.5) compared to Groups A and B (p<0.038 and p<0.030, respectively), indicating a potential impact on ovarian reserve and hormonal response. Group C also had a higher number of oocytes retrieved (13.7±6.4) and mature oocytes (MII oocytes) (12.0±7.7) compared to Groups A (12.4±7.0 and 8.8±6.0) and B (12.5±6.4 and 8.6±5.3) (p<0.039 and p<0.013, respectively). Fertilization rates were also significantly higher in Group C (9.0±6.2) compared to Group A (6.8±5.3) (p<0.047). The day of embryo vitrification differed significantly among the groups, with Group C showing the highest proportion of embryos vitrified on Day 5 (57.3%), followed by Group B (48.3%) and Group A (55.2%) (p<0.046). However, there were no significant differences in the number of usable blasts, blast quality (A & B), or the number of blastocysts on Days 5 and 6 across the groups.

Table 1: Demographic information of the respondents.

Variables	Group A M±SD or N (%)	Group B M±SD or N (%)	Group C M±SD or N (%)	P value
Age (years)	31.2±4.6	31.9±5.3	31.1±4.6	0.700
BMI	26.4±4.8	27.4±5.9	26.4±5.0	0.680
Infertility type				
Primary	63 (72.4)	37 (61.7)	56 (68.3)	0.389
Secondary	24 (27.6)	23 (38.3)	26 (31.7)	
Infertility duration	6.5±3.9	7.0±4.5	6.3±3.6	0.249
AMH	3.3±2.6	3.7±2.9	5.7±4.1	0.008
Factor				
None	18 (20.8)	19 (31.6)	18 (21.9)	0.000
Cystic ovaries	0 (0.0)	4 (6.7)	0 (0.0)	
Diabetics	1 (1.1)	1 (1.7)	0 (0.0)	
Hypothyroid	3 (3.4)	7 (11.7)	3 (3.7)	
Low reserve	35 (40.2)	4 (6.7)	16 (19.5)	
PCO	20 (23.0)	19 (31.6)	37 (45.1)	
Tubal factor	10 (11.5)	4 (6.7)	8 (9.8)	
Combined	0 (0.0)	2 (3.3)	0 (0.0)	

Table 2: Clinical morphological characteristics of the respondents.

Variables	Group A M±SD or N (%)	Group B M±SD or N (%)	Group C M±SD or N (%)	P value
Follicles	11.9±5.4	12.4±5.8	-	0.882
Sperm H-normal	83 (95.4)	60 (100.0)	78 (95.1)	0.347
No of ET	17 (24.6)	6 (18.2)	6 (13.3)	0.323
FSH	235.6±27.8	231.1±25.9	238.1±33.6	0.038
HMG	150.7±97.1	129.6±82.2	137.9±91.5	0.030
Oocytes retrieval	12.4±7.0	12.5±6.4	13.7±6.4	0.039
MII Oocytes	8.8±6.0	8.6±5.3	12.0±7.7	0.013
Fertilization	6.8±5.3	6.6±4.5	9.0±6.2	0.047
Cleavage	6.7±5.3	-	4.6±6.1	0.181
Embryo vitrification	3.8±2.8	3.1±2.5	3.7±2.4	0.307
Usable blasts	3.8±2.9	3.3±2.8	4.0±3.4	0.677

Table 3 summarizes the clinical outcomes of IVF/ICSI among the three groups. The clinical pregnancy rate was significantly higher in Group A at 79.3%, compared to Group B (63.3%) and Group C (40.2%), with a p-value of 0.000. This suggests that Control oocytes were associated with better pregnancy outcomes. The miscarriage rate was significantly lower in Group C (1.2%) compared to Groups A (12.6%) and B (18.3%) (p<0.013), indicating that the oocytes with dark, severe coarse granules in PVS may reduce the risk of miscarriage. Regarding ongoing pregnancy, Group B had the highest rate at 33.3%, significantly higher than Group A (18.4%) and Group C (13.4%) (p<0.032). Lastly, the live birth rate was highest in Group A (60.9%) and Group C (63.6%), while it was

notably lower in Group B (18.4%), with a p-value of 0.000, highlighting that Control and dark severe coarse granules oocytes were associated with better live birth outcomes.

Table 4 presents the results of the ROC curve analysis for various variables in the context of coarse granules in oocytes. The area under the curve (AUC) values provides insight into the predictive value of each variable for successful IVF/ICSI outcomes. The AUC for oocyte retrieval (0.611) is statistically significant (p<0.022), suggesting a moderate ability to predict successful outcomes. The AUC for MII oocytes (0.683) is also significant (p<0.000), indicating a good predictive value for successful pregnancy outcomes. Fertilization had a similar AUC of 0.674 (p<0.002), demonstrating a strong predictive value. In contrast, the AUC for cleavage (0.385) was lower and only marginally significant (p<0.040), suggesting that it is a weaker predictor of IVF/ICSI success. The confidence intervals (95% CI) for all variables were reasonably narrow, indicating reliable estimates of the AUC values. Overall, MII oocytes and fertilization showed the highest predictive value among the variables analyzed.

Table 3: Clinical outcomes of IVF/ICSI among the respondents.

Variables	Group A	Group B	Group C	P value
Clinical pregnancy rate, N (%)	69 (79.3)	38 (63.3)	33 (40.2)	0.000
Miscarriage rate, N (%)	11 (12.6)	11 (18.3)	1 (1.2)	0.013
Ongoing pregnancy rate, N (%)	16 (18.4)	20 (33.3)	11 (13.4)	0.032
Live birth rate, N (%)	42 (60.9)	7 (18.4)	21 (63.6)	0.000

Table 4: ROC curve analysis during the presence of coarse granules.

Variables	AUC	SE	P value	95% CL	
				LB	UB
Oocytes retrieval	0.611	0.045	0.022	0.522	0.700
MII oocytes	0.683	0.044	0.000	0.597	0.768
Fertilization	0.674	0.051	0.002	0.573	0.775
Cleavage	0.385	0.056	0.040	0.276	0.495

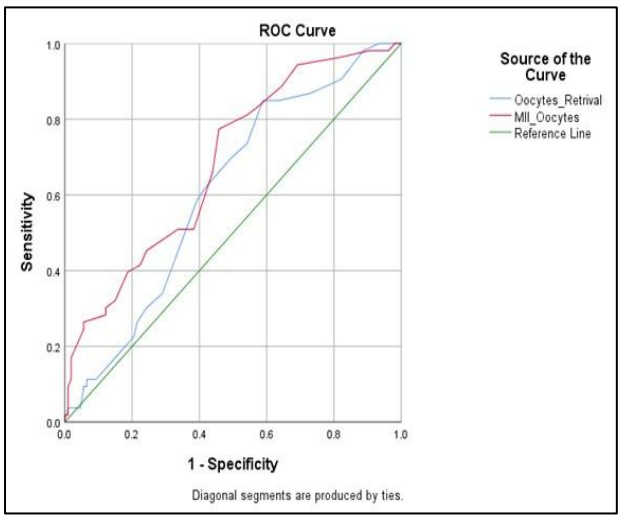

Figure 2: ROC curve for oocyte retrieval and MII oocytes during the presence of coarse granule.

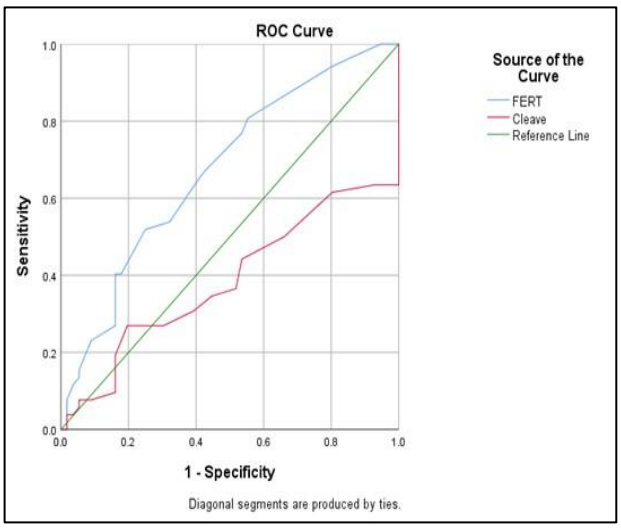

Figure 3: ROC curve for fertilization and cleavage during the presence of coarse granules.

Figure 2 shows the ROC curve for Oocyte Retrieval and MII Oocytes. The ROC curve for Oocyte Retrieval has an AUC of 0.611, suggesting a moderate ability to predict successful IVF outcomes. MII Oocytes demonstrated a higher AUC of 0.683, indicating a stronger predictive value for the success of the IVF/ICSI cycle in cases oocytes with coarse granules in PVS.

Figure 3 illustrates the ROC curve for Fertilization and Cleavage. The Fertilization curve has an AUC of 0.674, suggesting that fertilization is a moderately strong predictor of success. In contrast, the Cleavage curve has a lower AUC of 0.385, indicating that cleavage is a relatively weak predictor in this context, though it is still statistically significant (p<0.040). Overall, the ROC

curves highlight that MII Oocytes and Fertilization are the most reliable predictors of IVF success when oocytes with coarse granules in PVS are present, while Cleavage has a lesser predictive value.

DISCUSSION

Our retrospective cohort research offers fresh perspectives on how coarse granules in PVS affects egg quality and the results of the subsequent IVF-ICSI cycle. These results show a strong relationship between the intensity of coarse granules in both clinical and embryological outcomes. The data demonstrate that Control oocytes (Group A) are associated with superior fertilization rates, clinical pregnancy rates, and live birth rates when compared to oocytes exhibiting moderate (Group B) or severe (Group C) granularity in PVS.

The correlation between higher AMH levels and coarse granules in the PVS is a significant finding, with Group C displaying the highest AMH levels (5.7±4.1, p=0.008). This implies that hyperstimulation linked to PCOS could be a factor in PVS granule development, which may have an impact on oocyte competence.[7,8] Higher rates of fertilization and implantation rates indicated that Group A, which had a lower incidence of PCOS, had better oocyte quality. This aligns with previous research indicating that excessive gonadotropin stimulation can lead to cytoplasmic dysmorphisms, thereby reducing developmental potential.[9]

Embryologically, oocytes from Group C exhibited higher retrieval and maturation rates (p=0.039 and p=0.013, respectively), yet their fertilization efficiency and cleavage rates were comparatively lower. These findings are further supported by the ROC curve analysis, which shows that MII oocytes and fertilization rates have a good predictive value for implantation success (AUC=0.683 and 0.674, respectively, p<0.01). It also suggests that although extremely granular oocytes have higher retrieval rates, their capacity to develop into viable blastocysts and competent embryos is greatly reduced.[10,11]

Clinical outcome analysis further supports this conclusion. The clinical pregnancy rate was highest in Group A (79.3%, p=0.000), while Group C demonstrated a markedly lower rate (40.2%). Interestingly, the miscarriage rate was lowest in Group C (1.2%), potentially reflecting the selection of only the most viable embryos for transfer from this group. Notably, the live birth rate was comparable between Group A (60.9%) and Group C (63.6%), raising the possibility that a subset of oocytes with severe granularity retains developmental potential. However, the significantly lower ongoing pregnancy rate in Group C (13.4%) suggests that despite implantation, sustained embryonic development may still be compromised.[12]

Mechanistically, cytoplasmic immaturity, abnormal zona pellucida architecture, and mitochondrial dysfunction have all been connected to the oocytes with presence of coarse granules in the PVS.[13] As shown in our study, these variables may work together to disrupt embryogenesis and decrease developmental competence. The requirement for optimal ovarian stimulation methods is further highlighted by the higher gonadotropin doses in Group C (FSH =238.1±33.6, HMG=137.9±91.5), which indicate that supraphysiological stimulation may worsen granular development.

CONCLUSION

Our research highlights the important influence of PVS granularity on clinical pregnancy outcomes, oocyte competence, and fertilization potential. Even though oocytes with dark, severe coarse granules in PVS are linked to higher oocyte retrieval and maturation, they significantly impair the ability of the oocytes to fertilize and grow into embryos. These results highlight how crucial it is to carefully examine the oocytes' morphology before fertilization in order to maximize patient-specific ART approaches. Future studies should concentrate on clarifying the molecular basis of PVS granularity, namely its correlation with cytoplasmic maturation and mitochondrial integrity. To further increase ART success rates, ovarian stimulation procedures should be improved to reduce the occurrence of granular formations in PVS. Clinically, combining AI-assisted embryo selection with improved imaging may yield a more accurate prediction model for choosing high-quality oocytes, improving live birth outcomes in ART cycles.

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REFERENCES

1. Ozturk S. Selection of competent oocytes by morphological criteria for assisted reproductive technologies. Mole Reproduct Develop. 2020;87(10):1021-36.
2. Nikiforov D, Grøndahl ML, Hreinsson J, Andersen CY. Human oocyte morphology and outcomes of infertility treatment: a systematic review. Reproduct Sci. 2022;29(10):2768-85.
3. Bartolacci A, Intra G, Coticchio G, dell'Aquila M, Patria G, Borini A. Does morphological assessment predict oocyte developmental competence? A systematic review and proposed score. J Assist Reproduct Genet. 2022;39(1):3-17.
4. Franks S, Hardy K. What causes anovulation in polycystic ovary syndrome?. Curr Opin Endocr Metabol Res. 2020;12:59-65.
5. Thompson CJ, Costello RW, Crowley RK. Management of hypothalamic disease in patients with craniopharyngioma. Clin Endocrinol. 2019;90(4):506-16.

6. Hassan-Ali H, Hisham-Saleh A, El-Gezeiry D, Baghdady I, Ismaeil I, Mandelbaum J. Perivitelline space granularity: a sign of human menopausal gonadotrophin overdose in intracytoplasmic sperm injection. Human reproduction (Oxford, England). 1998;13(12):3425-30.
7. Farhi J, Nahum H, Weissman A, Zahalka N, Glezerman M, Levran D. Coarse granulation in the perivitelline space and IVF-ICSI outcome. J Assis Reproduct Genet. 2002;19(12):545-9.
8. Bulgurcuoglu-Kuran S, Altun A, Karakus FN, Kotil T, Ozsait-Selcuk B. Ultrastructure of coarse granules in the perivitelline space and association with ovulation induction protocols. JBRA Assist Reproduct. 2023;27(4):660.
9. Peng J, Zou W, Zhu L, Guo X, Zhang J, Li H. A case report of a successful pregnancy after intracytoplasmic sperm injection when all oocytes contained abnormal inclusions in the perivitelline space. Zygote. 2025;33(2):74-9.
10. Hu J, Molinari E, Darmon S, Zhang L, Patrizio P, Barad DH, et al. Predictive value of cytoplasmic granulation patterns during in vitro fertilization in metaphase II oocytes: Part I, poor-prognosis patients. Fertil Steril. 2021;116(2):431-43.
11. Rienzi L, Balaban B, Ebner T, Mandelbaum J. The oocyte. Human Reproduct. 2012;27(suppl_1):i2-1.
12. Shi W, Xu B, Wu LM, Jin RT, Luan HB, Luo LH, et al. Oocytes with a dark zona pellucida demonstrate lower fertilization, implantation and clinical pregnancy rates in IVF/ICSI cycles. PloS one. 2014;9(2):e89409.
13. Kim TE, Lee HK, Jee BC. Clinical and laboratory factors associated with the presence of dysmorphic oocytes in intracytoplasmic sperm injection cycles. Clin Experim Reproduct Medi. 2023;50(4):270.

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