RESEARCH PAPER

A Comparative Evaluation of 3D-Printed Versus Conventional Cumulus Denudation Pipette in Oocyte Denudation Efficacy and Safety: An Experimental Study

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ABSTRACT

Introduction: Cumulus cell removal (denudation) is an essential step in assisted reproductive techniques for accurate oocyte assessment and successful intracytoplasmic sperm injection (ICSI). Conventional denudation pipettes are effective but often costly and less accessible in resource-limited settings. Advances in three-dimensional (3D) printing technology provide a potential low-cost and customizable alternative for developing laboratory instruments.

Methodology: This experimental comparative study included 60 cumulus–oocyte complexes (COCs), which were randomly divided into two groups: Group A (denudation using a 3D-printed pipette) and Group B (conventional pipette). The 3D-printed pipette was designed using computer-aided design (CAD) software and fabricated with appropriate tip dimensions. Outcome measures included time taken for denudation, efficiency of cumulus cell removal, ease of handling, structural integrity, surface characteristics, oocyte survival rate, and incidence of oocyte damage. Statistical analysis was performed with significance set at $p < 0.05$.

Results: The 3D-printed pipette demonstrated comparable performance to the conventional pipette. The mean denudation time was 2.8 ± 0.6 minutes in Group A and 2.6 ± 0.5 minutes in Group B ($p = 0.181$). Complete cumulus removal was achieved in 86.7% and 90% of cases respectively ($p = 0.641$). Ease of handling was rated very easy in 60% of the 3D-printed group and 66.7% of the conventional group. Structural integrity was high in both groups with no breakage observed. Surface smoothness was slightly better in conventional pipettes. Oocyte survival rates were 90% and 93.3% ($p = 0.721$), with minimal damage in both groups.

Conclusion: The 3D-printed cumulus denudation pipette is a safe, effective, and cost-efficient alternative to conventional pipettes, with promising applications in resource-limited ART settings.

Keywords: 3D printing, cumulus denudation, oocyte, assisted reproductive technology, ICSI, pipette design, reproductive medicine.

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INTRODUCTION

The field of assisted reproductive technology (ART) has advanced significantly over recent decades, offering effective solutions for infertility, which affects approximately 10–15% of couples globally [1]. Innovations in reproductive medicine, including in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), have improved success rates; however, these techniques rely heavily on precise laboratory procedures and high-quality instruments for optimal outcomes [2]. The accuracy and reliability of laboratory tools are critical for successful fertilization and embryo development.

A key step in ART is cumulus denudation, the removal of cumulus cells surrounding the oocyte. These cells, forming the cumulus–oocyte complex (COC), are essential for oocyte maturation and metabolic support [3]. However, their removal is necessary during ICSI to allow proper visualization and assessment of oocyte maturity and morphology [4]. This process typically involves enzymatic digestion using hyaluronidase followed by mechanical stripping with specialized pipettes, requiring precision to avoid oocyte damage [5].

Conventional denudation pipettes are produced using micropipette pullers and microforges, which demand technical expertise and are time-consuming [6]. Additionally, commercially available pipettes are expensive and lack flexibility for customization, posing challenges for laboratories with limited resources [7]. These limitations highlight the need for cost-effective and adaptable alternatives.

Three-dimensional (3D) printing, or additive manufacturing, has emerged as a transformative technology in biomedical engineering. It enables rapid, layer-by-layer fabrication of objects from digital designs, allowing customization, reduced production time, and lower costs [8,9]. In medicine, 3D printing has been widely applied in the development of prosthetics, implants, surgical guides, and laboratory equipment [10]. Its integration into research has facilitated the creation of precise and reproducible microtools tailored to specific applications [11].

Advanced techniques such as stereolithography (SLA) and fused deposition modeling (FDM) allow high-resolution fabrication of micro-scale devices with excellent reproducibility [12]. These technologies have enabled the development of specialized tools for cell culture, microfluidics, and biological manipulation at reduced cost and time [13]. In ART, 3D printing offers the potential to fabricate customized denudation pipettes with specific tip diameters and ergonomic designs suitable for oocyte handling [14].

Moreover, 3D printing reduces dependence on expensive commercial equipment, enhancing accessibility, especially in resource-limited settings [15]. Rapid prototyping allows iterative design improvements, promoting innovation and optimization of laboratory tools [16]. However, factors such as material biocompatibility, sterilization, and surface smoothness must be carefully considered to ensure safety and functionality [17]. Validation of these tools against conventional methods is essential to establish their reliability [18].

Given the increasing demand for affordable and customizable laboratory instruments, 3D-printed microtools represent a promising alternative in ART laboratories. Therefore, this study aims to design, fabricate, and evaluate a 3D-printed cumulus denudation pipette and assess its feasibility as a cost-effective and reliable tool in reproductive technology settings [19,20].

Aim

- To design, fabricate, and evaluate a cost-effective, reproducible, and functional cumulus denudation pipette using 3D printing technology for use in assisted reproductive technologies (ART).

Objective

1. To design a cumulus denudation pipette using computer-aided design (CAD) software with dimensions suitable for oocyte manipulation
2. To fabricate the designed pipette using a compatible 3D printing material and technology (e.g., SLA or FDM).
3. To assess the structural integrity, precision, and usability of the 3D printed pipette in a laboratory setting.

METHODOLOGY

The present study was conducted in two phases: product development and experimental evaluation. The first phase involved the design and fabrication of a 3D-printed cumulus denudation pipette using a laboratory-based experimental approach. The objective was to develop a cost-effective, reproducible, and functionally efficient alternative to conventional pipettes used in assisted reproductive technology (ART), while ensuring safety and precision during oocyte handling. The second phase consisted of a comparative experimental study to evaluate the performance, safety, and feasibility of the developed pipette.

Conceptualization and Design

The design of the pipette was conceptualized based on standard commercially available denudation pipettes used in ART laboratories. Key parameters considered included appropriate internal diameter for effective removal of cumulus cells, gradual tapering to minimize shear stress, smooth internal and external surfaces to prevent mechanical damage, and adequate length for ergonomic handling. The aim was to replicate the functional characteristics of conventional pipettes while allowing customization.

Computer-Aided Design and Modeling

The pipette was digitally designed using computer-aided design (CAD) software (AutoCAD). A detailed three-dimensional model incorporating lumen diameter, tapering angle, and tip geometry was developed. The design was exported in Standard Tessellation Language (STL) format and refined through multiple iterations to optimize fluid dynamics and handling characteristics.

Material Selection and 3D Printing

Biocompatible and non-toxic materials such as polylactic acid (PLA) were considered, with PLA selected due to its cost-effectiveness, ease of printing, and acceptable safety profile. The STL file was processed using slicing software to generate G-code, and fabrication was performed using a high-resolution fused deposition modeling (FDM) 3D printer. Printing parameters, including layer height (0.1–0.2 mm), nozzle diameter, temperature, and speed, were optimized to ensure precision and smooth surface finish. Multiple pipettes were produced to ensure consistency.

Post-Processing and Quality Assessment

Following fabrication, pipettes underwent post-processing, including removal of support structures, polishing, and microscopic inspection. Special attention was given to smoothing the tip and internal lumen to minimize friction and prevent oocyte damage. Dimensional verification was performed using digital calipers and microscopy to assess internal diameter, tip uniformity, surface smoothness, and structural integrity. Only pipettes meeting predefined criteria were selected.

Sterilization and Pilot Testing

Sterilization was performed using ethylene oxide or ultraviolet radiation, depending on material compatibility. Pilot testing was conducted in a controlled laboratory environment to assess ease of handling, suction control, effectiveness of cumulus cell removal, and oocyte integrity. Feedback from embryologists was incorporated to refine the final design, which was then standardized for further evaluation.

Study Setting and Population

The experimental study was conducted over a period of 12 months from January 2024 to January 2025 at Saveetha Medical College and Hospital. A total of 60 cumulus–oocyte complexes (COCs) were included using a consecutive sampling technique. Samples were obtained from discarded human oocytes and animal oocytes (bovine or murine) used for research purposes following ethical approval.

Inclusion and Exclusion Criteria

Inclusion criteria comprised availability of suitable oocytes, use of high-resolution 3D printers, pipette tip diameter between 135–150 µm, and involvement of trained laboratory personnel. Exclusion criteria included defective pipettes, non-biocompatible materials, damaged or degenerated oocytes, pre-denuded oocytes, and pipettes causing mechanical damage.

Study Groups and Procedure

The samples were divided equally into two groups: Group A (3D-printed pipette) and Group B (conventional pipette). All procedures were performed under standardized laboratory conditions by trained embryologists. COCs were maintained in appropriate culture media, and denudation was carried out using enzymatic treatment with hyaluronidase followed by mechanical pipetting. Post-procedure evaluation was performed using an inverted microscope to assess completeness of denudation and oocyte morphology.

Outcome Measures and Data Collection

Parameters assessed included structural characteristics (tip diameter, surface smoothness, integrity), functional performance (time taken, efficiency of cumulus removal, ease of handling), and biological safety (oocyte survival and damage rates, zona pellucida integrity). Cost analysis was also performed. Quantitative data included measurements and percentages, while qualitative data included feedback from embryologists on usability and ergonomics.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26. Continuous variables were expressed as mean and standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were made using independent t-test and Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 cumulus–oocyte complexes were included in the study. These were equally distributed between the two groups, with 30 oocytes (50%) in Group A, where the 3D-printed cumulus denudation pipette was used, and 30 oocytes (50%) in Group B, where the conventional pipette was used.

The structural evaluation demonstrated that both pipettes exhibited comparable dimensional and physical characteristics suitable for oocyte manipulation. The mean tip diameter of the 3D-printed pipette was 142.6 ± 3.8 µm, while the conventional pipette measured 140.3 ± 2.9 µm. The observed ranges (135–150 µm for 3D-printed and 136–145 µm for conventional pipettes) were within the acceptable limits, indicating adequate dimensional accuracy in both groups.

Assessment of structural integrity showed that the majority of pipettes maintained an intact structure, with 28 (93.3%) in the 3D-printed group and 29 (96.7%) in the conventional group. Minor deformation was noted in 2 (6.7%) and 1 (3.3%) pipettes, respectively, while no breakage was observed in either group, reflecting good mechanical stability during use. Surface smoothness evaluation revealed that 24 (80%) of the 3D-printed pipettes were smooth, 5 (16.7%) were moderately smooth, and 1 (3.3%) exhibited rough edges. In comparison, conventional pipettes demonstrated slightly superior surface characteristics, with 28 (93.3%) classified as smooth and 2 (6.7%) as moderately smooth, and no instances of rough edges. Overall, both pipettes showed satisfactory structural properties, although conventional pipettes had a marginal advantage in surface finish. (Table 1)

Table 1: Structural Evaluation of Pipettes

Parameter	**Subcategory**	**3D Printed Cumulus Denudation Pipette**	**Conventional Cumulus Denudation Pipette**
Tip Diameter (µm)	Mean	142.6 ± 3.8	140.3 ± 2.9
	Range	135–150	136–145
Structural Integrity	Intact Structure	28 (93.3%)	29 (96.7%)
	Minor Deformation	2 (6.7%)	1 (3.3%)
	Breakage	0 (0%)	0 (0%)
Surface Smoothness	Smooth	24 (80%)	28 (93.3%)
	Moderately Smooth	5 (16.7%)	2 (6.7%)
	Rough Edges	1 (3.3%)	0 (0%)

The functional performance analysis demonstrated that both pipettes showed comparable outcomes across all assessed parameters. The mean time required for cumulus denudation was 2.8 ± 0.6 minutes in the 3D-printed pipette group and 2.6 ± 0.5 minutes in the conventional pipette group, with no statistically significant difference observed ($p = 0.181$), indicating similar procedural efficiency.

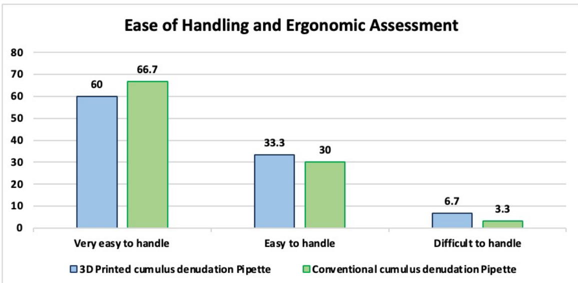
In terms of effectiveness, complete removal of cumulus cells was achieved in 26 (86.7%) cases in the 3D-printed group and 27 (90%) cases in the conventional group. Partial removal was observed in 3 (10%) and 2 (6.7%) cases, respectively, while incomplete removal occurred in 1 (3.3%) case in both groups. The difference between the groups was not statistically significant ($p = 0.641$), suggesting comparable efficiency in cumulus cell removal.

Assessment of ease of handling revealed that the majority of pipettes in both groups were user-friendly. In the 3D-printed group, 18 (60%) were rated as very easy to handle, 10 (33.3%) as easy, and 2 (6.7%) as difficult. In comparison, the conventional group showed slightly better ratings, with 20 (66.7%) categorized as very easy, 9 (30%) as easy, and 1 (3.3%) as difficult. Overall, both pipettes demonstrated good ergonomic performance, with a marginal advantage observed in conventional pipettes. (Table 2, Figure 1)

Table 2: Functional Performance of Pipettes

Parameter	**Subcategory**	**3D Printed Cumulus Denudation Pipette**	**Conventional Cumulus Denudation Pipette**
Time for Denudation (minutes)	Mean	2.8 ± 0.6	2.6 ± 0.5
Efficiency of Cumulus Removal	Complete Removal	26 (86.7%)	27 (90%)
	Partial Removal	3 (10%)	2 (6.7%)
	Incomplete Removal	1 (3.3%)	1 (3.3%)

Figure 1: Ease of Handling and Ergonomic Assessment



The biological safety evaluation showed comparable outcomes between the two groups. In the 3D-printed pipette group, 27 oocytes survived and 3 were damaged, resulting in a survival rate of 90%, whereas in the conventional pipette group, 28 oocytes survived and 2 were damaged, with a survival rate of 93.3%. The difference between the groups was not statistically significant ($p = 0.721$), indicating similar safety profiles.

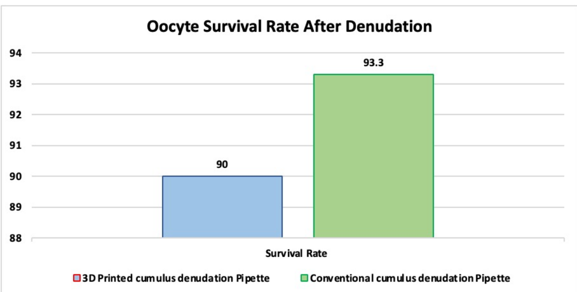
Regarding the type of damage, zona pellucida damage was observed in 2 (6.7%) cases in the 3D-printed group and 1 (3.3%) case in the conventional group, while cytoplasmic damage occurred in 1 (3.3%) case in both groups. No cases of oocyte degeneration were reported in either group, suggesting minimal overall damage during the procedure.

Assessment of zona pellucida integrity revealed that most oocytes remained structurally intact, with 27 (90%) in the 3D-printed group and 28 (93.3%) in the conventional group. Minor disruption was observed in 3 (10%) and 2 (6.7%) cases, respectively, with no instances of severe damage in either group. These findings indicate that both pipettes effectively preserved oocyte structure and integrity during cumulus denudation. (Table 3, Figure 2)

Table 3: Biological Safety Evaluation of Pipettes

Parameter	**Subcategory**	**3D Printed Cumulus Denudation Pipette**	**Conventional Cumulus Denudation Pipette**
Oocyte Survival	Survived (n)	27	28
	Damaged (n)	3	2
	Survival Rate (%)	90%	93.3%
Oocyte Damage Type	Zona Pellucida Damage	2 (6.7%)	1 (3.3%)
	Cytoplasmic Damage	1 (3.3%)	1 (3.3%)
	Degeneration	0 (0%)	0 (0%)
Zona Pellucida Integrity	Intact	27 (90%)	28 (93.3%)
	Minor Disruption	3 (10%)	2 (6.7%)
	Severe Damage	0 (0%)	0 (0%)

Figure 2: Oocyte Survival Rate After Denudation



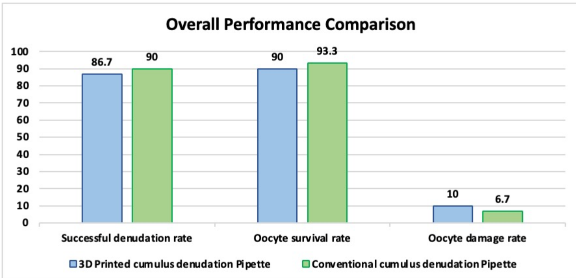
The cost per pipette was ₹120 for the 3D-printed pipette and ₹850 for the conventional pipette. The manufacturing cost was low for the 3D-printed pipette compared to high for the conventional pipette. The 3D-printed pipette was reusable after sterilization, while the conventional pipette had limited reuse. The average cost per procedure was ₹40 for the 3D-printed pipette and ₹280 for the conventional pipette, demonstrating significant cost advantage. (Table 4)

Table 4: Cost Comparison of Pipettes

Parameter	**3D Printed cumulus denudation Pipette**	**Conventional cumulus denudation Pipette**
Cost per pipette (₹)	120	850
Manufacturing cost	Low	High
Reusability	Reusable after sterilization	Limited reuse
Average cost per procedure (₹)	40	280

The mean denudation time was 2.8 minutes for the 3D-printed pipette and 2.6 minutes for the conventional pipette ($p = 0.181$). The successful denudation rate was 86.7% and 90% ($p = 0.641$), oocyte survival rate was 90% and 93.3% ($p = 0.721$), and oocyte damage rate was 10% and 6.7% ($p = 0.588$), respectively. None of these differences were statistically significant, indicating comparable overall performance. (Figure 3)

Figure 3: Overall Performance Comparison



Among embryologists, 50% rated handling comfort as excellent, 33.3% as good, 13.3% as average, and 3.4% as poor. Precision was rated excellent by 46.7%, good by 36.7%, average by 13.3%, and poor by 3.3%. Ergonomic design received excellent ratings from 53.5%, and overall usability was rated excellent by 50% of participants. This indicates high user satisfaction with the 3D-printed pipette. (Figure 1,2)

Figure 4: Embryologist Feedback on 3D-Printed Pipette

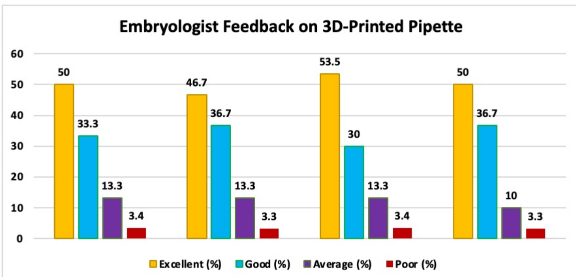
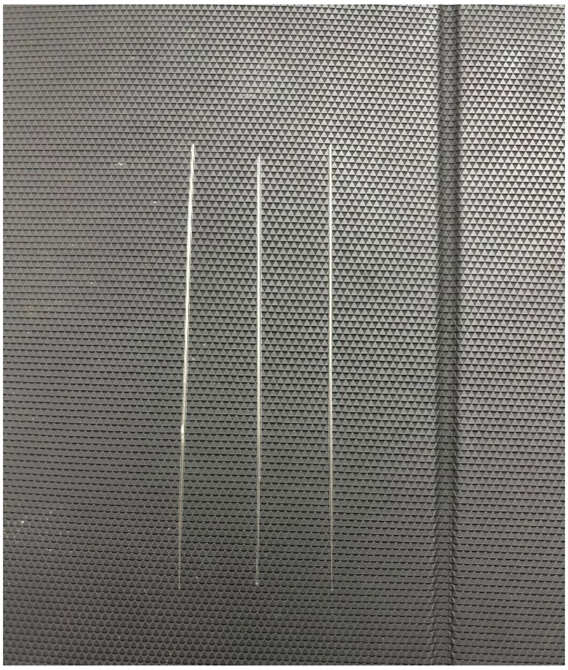


Figure 5: Fabricated 3D printed cumulus denudation pipette.



DISCUSSION

The present study evaluated the feasibility, performance, and safety of 3D-printed pipettes in comparison with conventional pipettes for oocyte denudation in assisted reproductive technology (ART), and the findings demonstrate that 3D-printed pipettes perform comparably across structural, functional, and biological parameters. These results are consistent with the growing body of literature supporting the application of additive manufacturing in biomedical and laboratory settings as a reliable and cost-effective alternative to traditional tools.

The mean tip diameter of the 3D-printed pipette (142.6 ± 3.8 µm) was comparable to that of the conventional pipette (140.3 ± 2.9 µm), and both were within the optimal range of 135–150 µm recommended for oocyte manipulation. This aligns with the findings of Gordon [5], who emphasized that maintaining appropriate pipette diameter is essential to balance efficient cumulus removal and preservation of oocyte integrity. Similar observations were reported by Weikert et al. [21], who highlighted that even minor variations in diameter can influence shear forces; however, the differences observed in the present study were minimal and clinically insignificant. Advances in 3D printing technology, as described by Wang et al. and Chua and Leong [6,8], have enabled micron-level precision, supporting the dimensional accuracy observed in this study.

Structural integrity was maintained in the majority of pipettes in both groups, with no breakage observed, which is consistent with previous studies demonstrating improved mechanical strength of 3D-printed biomedical devices. Ngo et al. [20] and Waheed et al. [19] reported that advancements in printing materials and post-processing techniques significantly enhance durability and reduce deformation in 3D-printed instruments. Similarly, Capel et al. [7] demonstrated that 3D-printed laboratory tools can achieve structural reliability comparable to conventionally manufactured devices. The slightly higher rate of minor deformation in the 3D-printed group in the present study is likely due to inherent material properties but does not affect overall functionality.

Surface smoothness was marginally better in conventional pipettes, which is in agreement with earlier reports highlighting limitations of layer-by-layer fabrication in additive manufacturing. Bavister [22] emphasized that surface irregularities can increase mechanical stress on oocytes, potentially affecting viability. However, studies by Ngo et al. [20] and Waheed et al. [19] have shown that modern post-processing techniques significantly improve surface finish. In the present study, despite minor surface irregularities, no significant increase in oocyte damage was observed, suggesting that the surface quality of 3D-printed pipettes is clinically acceptable.

The functional performance of both pipettes was comparable, with no significant difference in the time required for cumulus denudation. This finding is supported by Gardner et al. [23] and Rienzi et al. [24], who emphasized that procedural efficiency is critical in ART to minimize oocyte exposure to suboptimal conditions. The small difference in denudation time observed in this study is unlikely to have clinical relevance. Furthermore, the efficiency of cumulus cell removal was similar between the groups, which is consistent with the observations of Rienzi et al. [24], who highlighted that effective denudation is essential for accurate assessment of oocyte maturity and successful fertilization. The comparable performance indicates that 3D-printed pipettes can replicate the functional capabilities of conventional instruments.

Biological safety outcomes, including oocyte survival rate and damage rate, were also comparable between the two groups. The survival rate of 90% in the 3D-printed group and 93.3% in the conventional group is consistent with acceptable ART laboratory standards. Bavister [22] and Swain and Smith [26] have emphasized that minimizing mechanical stress during oocyte handling is crucial for maintaining viability. The low incidence of zona pellucida and cytoplasmic damage observed in this study supports the conclusion that 3D-printed pipettes do not increase the risk of oocyte injury. Similar findings have been reported in studies evaluating the safety of 3D-printed biomedical devices, where no significant adverse biological effects were observed when appropriate materials and processing techniques were used [19,20].

The integrity of the zona pellucida was preserved in the majority of oocytes in both groups, which is essential for successful fertilization and embryo development. Gardner et al. [23] and Cohen and Malter [63] have highlighted the importance of maintaining zona integrity during micromanipulation procedures. The comparable outcomes observed in this study suggest that the mechanical forces exerted by 3D-printed pipettes are within safe limits, further supporting their suitability for ART applications.

One of the most significant findings of this study is the substantial cost reduction associated with 3D-printed pipettes. The cost per pipette and per procedure was markedly lower compared to conventional pipettes, which aligns with findings from Chua and Leong [8] and Ngo et al. [20], who reported that additive manufacturing enables low-cost production with minimal material wastage. Niederberger et al. [25] also emphasized the importance of cost reduction in improving access to ART services, particularly in resource-limited settings. The ability to reuse 3D-printed pipettes after sterilization further enhances their economic advantage.

Overall, the findings of this study are consistent with existing literature demonstrating that 3D-printed biomedical tools can achieve performance and safety comparable to conventional devices. The absence of statistically significant differences across key parameters indicates that 3D-printed pipettes are a viable alternative for oocyte denudation. Furthermore, as highlighted by Swain and Smith [26], operator skill and laboratory conditions often play a more significant role in determining ART outcomes than minor variations in instrument design. Therefore, the successful performance of 3D-printed pipettes in this study supports their potential for integration into routine ART practice, with opportunities for further refinement and customization based on user feedback and technological advancements.

Limitations

The present study has several limitations. The relatively small sample size may limit statistical power and generalizability. Outcomes were influenced by operator skill, introducing potential bias. The study evaluated only short-term outcomes such as denudation efficiency, oocyte survival, and damage, without assessing long-term reproductive outcomes like fertilization, embryo quality, implantation, or pregnancy rates. Surface smoothness was assessed qualitatively without advanced techniques such as profilometry. Variability in 3D printing and post-processing may have affected consistency. Lack of blinding could introduce bias. Additionally, comprehensive cost–benefit analysis, durability, repeated usage, and ergonomic aspects were not fully evaluated.

Future direction

Future research should include larger multi-center studies to improve the reliability and generalizability of findings. Long-term clinical outcomes such as fertilization rates, embryo quality, implantation, and pregnancy rates need to be evaluated. Standardization of 3D printing and post-processing protocols is essential to ensure consistency. Advanced surface finishing techniques and precise measurement tools should be incorporated to improve quality. Further studies should assess biocompatibility and sterilization effects. Minimizing operator bias through blinding and multiple users is recommended. Comprehensive cost-effectiveness analysis, along with evaluation of durability, reusability, and design optimization, will help establish the practical applicability of 3D-printed pipettes in ART laboratories.

CONCLUSION

The present study demonstrates that the 3D-printed cumulus denudation pipette is a safe, effective, and feasible alternative to the conventional pipette used in assisted reproductive techniques. The performance of the 3D-printed device was comparable to that of the standard pipette in terms of efficiency of cumulus cell removal, ease of handling, and preservation of oocyte integrity. Importantly, the use of the 3D-printed pipette did not compromise oocyte survival or increase the risk of mechanical damage, indicating its suitability for delicate micromanipulation procedures. Although minor differences in surface smoothness and handling characteristics were observed, these did not translate into clinically significant outcomes. The findings highlight the potential of 3D printing technology as a cost-effective and customizable approach for developing laboratory instruments in reproductive medicine. This innovation may be particularly beneficial in resource-limited settings, where access to specialized equipment is often restricted. Overall, the study supports the adoption of 3D-printed pipettes as a reliable alternative to conventional devices, with scope for further refinement and large-scale validation in clinical practice.

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Supplementary images

Figure A: High-Precision Micro-Tip Attachment for Gentle and Controlled Cumulus Cell Denudation

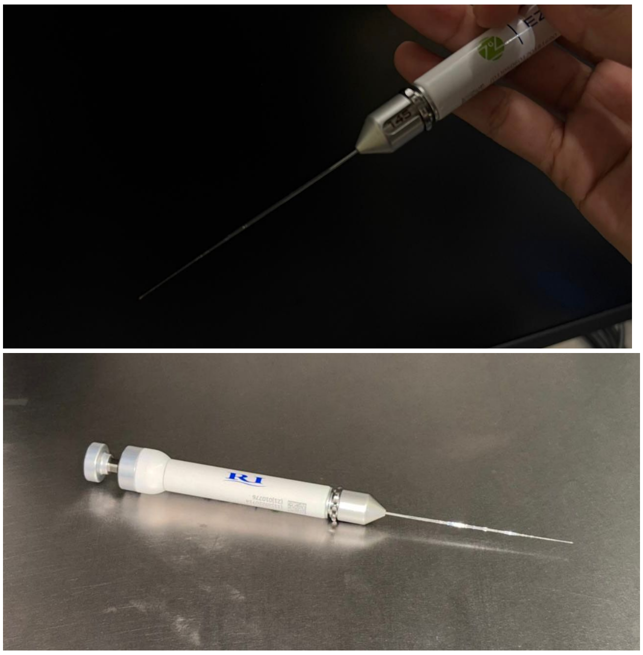

Figure B: Stereozoom Microscope Setup for Oocyte Handling and Cumulus Cell Denudation

Figure C: Manual Handling of Oocytes Using a Denudation Pipette Under Stereozoom Microscopy

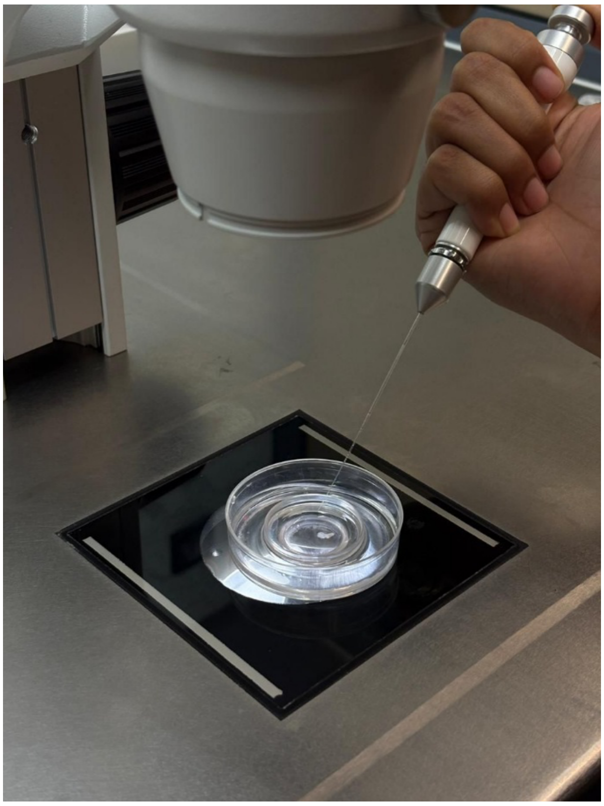

Figure D: Microscopic View of Oocyte During Cumulus Cell Denudation Using a Micro-Pipette