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Clinical feasibility and cost efficiency of perinatal mesenchymal stem cell production under GMP conditions

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Perinatal tissues such as umbilical cord, amniotic fluid, amniotic membrane, and placenta contain mesenchymal stem cells (MSCs) with clinical potential; however, a direct comparison of these sources under Good Manufacturing Practice (GMP) conditions remains limited. To evaluate and compare perinatal tissue types in terms of viable MSC yield, sterility, and GMP-adjusted processing cost in order to identify practically applicable sources for clinical-grade biobanking. A total of 160 perinatal tissue samples were collected from 32 term pregnancies during elective cesarean delivery. Standardized GMP protocols were applied for MSC isolation, sterility screening using automated BACTEC™ culture systems, and immunophenotypic characterization in accordance with ISCT criteria. Multivariate linear regression was used to identify independent predictors of MSC yield. Cost modeling included reagents, labor, and cryostorage within a laboratory-scale GMP setting. Umbilical cord tissue yielded the highest number of viable MSCs ($6.5 \times 10^6 \pm 0.8$ cells/sample), followed by amniotic fluid ($5.8 \times 10^6 \pm 0.6$). Amniotic fluid exhibited the lowest contamination rate (3%), whereas placental tissues demonstrated higher microbial burden (18–21%). Tissue type was the strongest predictor of MSC yield ($\beta = 0.61$, $p < 0.001$). Normalized cost analyses indicated that umbilical cord and amniotic fluid offered the most favorable yield-to-cost profiles. Under current GMP conditions, umbilical cord and amniotic fluid appear to provide the most balanced combination of MSC yield, sterility, and processing cost. These findings support a practical framework for tissue selection and workflow optimization in perinatal MSC biobanking and translational regenerative applications.

Keywords Mesenchymal stem cells, Umbilical cord, Amniotic fluid, Placenta, Cost-effectiveness, Perinatal tissue, Regenerative medicine, Sterility

Regenerative medicine has evolved into a transformative discipline that leverages stem cell–based strategies to repair, replace, or regenerate damaged tissues. Stem cells are defined by their capacity for self-renewal, multilineage differentiation, and immunomodulation, positioning them as central tools in modern cellular therapy[1]. Among various stem cell populations, mesenchymal stem cells (MSCs) have received extensive attention due to their ease of isolation, in vitro expandability, and low immunogenicity compared to embryonic stem cells[2,3].

However, traditional MSC sources such as bone marrow and adipose tissue present clinical and ethical limitations. Their collection involves invasive procedures, potential donor-site morbidity, and age-related declines in stem cell yield and regenerative capacity[4,5]. These challenges have driven the search for alternative, non-invasive, and ethically acceptable sources of MSCs that could sustain scalable production for clinical use.

Perinatal tissues—including the umbilical cord, amniotic fluid, amniotic membrane, and placenta—have emerged as abundant, biologically rich, and ethically neutral reservoirs of fetal-derived MSCs, often discarded as medical waste following delivery[6,7]. Their origin from extraembryonic fetal structures provides high proliferative potential, robust paracrine signaling, and low expression of Human Leukocyte Antigen (HLA) class II molecules, enabling potential allogeneic transplantation without significant immune rejection[8].

Despite their promise, the clinical translation of perinatal MSCs remains limited. Existing studies have typically focused on biological characterization or differentiation capacity under research-grade conditions,

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whereas comparative investigations that simultaneously address MSC yield, sterility, and true GMP-adjusted cost per viable cell are extremely limited in the literature. Furthermore, the transition from research-grade to GMP-compliant production introduces logistical challenges such as tissue collection timing, contamination control, and economic feasibility of large-scale processing[9–11].

From a translational perspective, one of the most underexplored aspects of perinatal stem cell utilization involves the coordination between obstetric services and GMP laboratories. The safe procurement, labeling, sterile transfer, and standardized processing of birth tissues require precise synchronization between clinical and manufacturing units. Variables such as delivery mode, tissue handling time, and temperature regulation can markedly influence cell viability and contamination risk[10,12,13]. However, few investigations have quantitatively evaluated how these operational parameters affect both sterility and production cost within GMP workflows.

The present study was designed to address this gap by conducting a prospective, GMP-integrated comparison of perinatal tissues—specifically amniotic fluid, amniotic membrane, umbilical cord, and placental tissues—in terms of (i) MSC yield, (ii) microbial contamination rate, and (iii) standardized cost per million viable MSCs. Additionally, flow cytometric confirmation of MSC phenotype according to International Society for Cellular Therapy (ISCT) criteria and multivariate analysis controlling for maternal and procedural variables were incorporated to enhance scientific rigor and reproducibility.

To the best of our knowledge, no previous study has combined biological output, sterility assessment, and GMP-based cost modeling into a single clinically oriented feasibility framework. Rather than claiming superiority of one tissue source, this study aims to provide objective, data-driven benchmarking to support rational tissue selection for clinical-scale biobanking. This approach offers a pragmatic decision-making model, contributing to the sustainable and standardized use of perinatal medical waste in regenerative medicine.

Materials and methods

Study design and ethical approval

This study was designed as a prospective, GMP-integrated observational investigation conducted between January and June 2023 at the Department of Obstetrics and Gynecology, Eskişehir Osmangazi University. Laboratory processing and stem cell characterization were performed at the Eskişehir Osmangazi University Stem Cell and Cellular Therapy Center (ESTEM), operating under ISO 7 cleanroom standards with validated SOPs and GMP documentation. Ethical approval was granted by the Institutional Clinical Research Ethics Committee of Eskişehir Osmangazi University (Approval No: 28; Date: August 3, 2023) and the study was conducted in accordance with the Declaration of Helsinki and national biomedical research regulations. Written informed consent was obtained from all participants prior to any sample collection.

Participant selection and tissue procurement

Study participants were selected among pregnant women with full-term, uncomplicated singleton pregnancies (≥ 37 weeks of gestation), who delivered either via cesarean section or spontaneous vaginal birth. Exclusion criteria included the presence of maternal infection, fetal malformation, placental abnormalities, or preterm labor. A total of 32 participants contributed five perinatal tissue types each, resulting in 160 tissue samples: amniotic fluid, amniotic membrane, umbilical cord (Wharton's jelly), placental fragments, and whole placenta (Supplementary Table S1). These tissues, typically regarded as medical waste, were immediately placed in sterile, pre-labeled transport containers and transferred to the GMP laboratory under cold chain conditions (4 °C) within 30–45 min to preserve cellular integrity. A limited number of vaginally obtained samples were evaluated solely for sterility comparison but excluded from GMP-grade production due to elevated microbial exposure.

Sterility assessment and preprocessing

All specimens underwent microbial contamination screening using the automated BACTEC™ FX (BD Diagnostics, USA) system. Prior to inoculation, each 1 cm^2 tissue segment was homogenized in 1 mL phosphate-buffered saline (PBS) under sterile conditions using a single-use homogenizer. The homogenate was then inoculated into aerobic and anaerobic culture bottles, following a validated procedure previously described by Arutyunyan et al. (2018)[14].

Samples exhibiting visible blood contamination were treated with ammonium chloride-based red blood cell lysis buffer (RBC lysis buffer, Sigma-Aldrich) for 5 min at room temperature before further processing.

Vaginally obtained samples were analyzed separately to confirm the higher contamination tendency of such tissues and excluded from downstream GMP processing. Negative (sterile blanks) and positive (Staphylococcus aureus, Candida albicans) controls were run in parallel for quality assurance (Supplementary Figure S1).

Isolation and culture of mesenchymal stem cells

Isolation and expansion of MSCs were performed under GMP conditions using tissue-specific protocols designed to ensure sterility, reproducibility, and high cell viability. All reagents were GMP-grade and handled in a Class II biosafety cabinet within ISO 7 cleanroom facilities. Procedures were standardized across tissue types to minimize operator-dependent variability.

For amniotic fluid, samples were centrifuged at 400 × g for 10 min, and the resulting cell pellet was resuspended in Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 (DMEM/F12, Gibco, Thermo Fisher Scientific, USA) supplemented with 10% fetal bovine serum (FBS, GMP-grade), 1% penicillin-streptomycin, and 2 mM L-glutamine. The cultures were incubated at 37 °C in 5% CO_2 and 95% humidity.

The amniotic membrane was separated from the chorion, washed with PBS, and subjected to enzymatic digestion using 0.25% collagenase type I (Sigma-Aldrich, USA) and 0.01% DNase I (Roche, Germany) for 90 min at 37 °C. The digested suspension was filtered through a 70 µm nylon mesh, and cells were seeded in T75 culture flasks (Corning, USA).

For the umbilical cord (Wharton's jelly), cords were rinsed to remove residual blood and dissected into 1–2 cm fragments. The tissue was digested with 0.25% collagenase type I and 0.01% DNase I at 37 °C for 90 min, followed by filtration through a 70 µm mesh. The resulting suspension was cultured in DMEM supplemented with 10% FBS and 1% antibiotic–antimycotic solution.

The placental tissue and placental fragments were minced into small pieces and digested enzymatically using collagenase I (0.25%) and DNase I (0.01%), similar to the amniotic membrane protocol. The cell suspension was then filtered, washed, and seeded into T75 flasks containing complete growth medium.

All cultures were maintained at 37 °C and 5% CO_2 and monitored daily under phase-contrast microscopy. Media were replaced every 48 h to eliminate debris and non-adherent cells. Passaging was performed at 80–90% confluence using TrypLE™ Express (Gibco, USA), and only cultures successfully expanded to passage 3 (P3) were included in downstream analyses.

Throughout all culture stages, sterility was continuously monitored by periodic sampling and mycoplasma testing. No cross-contamination was observed in any GMP-grade preparation.

Phenotypic characterization by flow cytometry

Phenotypic verification of MSC identity was conducted according to the ISCT criteria. Cells at passage 3 were stained with fluorochrome-conjugated monoclonal antibodies against CD73, CD90, and CD105 (positive markers) and CD34, CD45, and HLA-DR (negative markers). Analysis was carried out using a BD FACSCanto™ II flow cytometer (BD Biosciences, USA), recording at least 10,000 events per sample. The data were analyzed using FlowJo™ software (Tree Star Inc., USA). Cell populations expressing ≥ 95% of positive markers and ≤ 2% of negative markers were defined as MSCs. Representative gating strategies, histograms, and marker expression profiles are provided in Supplementary Figure S2. In addition, functional multipotency was confirmed through standard osteogenic, adipogenic, and chondrogenic differentiation protocols previously validated under GMP conditions[11,15] (Supplementary Figure S3).

Quantification of cell yield and proliferative capacity

Viable MSCs were quantified using the Countess II FL Automated Hemocytometer (Thermo Fisher) and trypan blue exclusion. For liquid tissues, yield was expressed as viable cells per milliliter, and for solid tissues, as viable cells per gram. Population doubling time (PDT) at passage 3 was calculated using: $PDT = T \times log2 / \log N2 - logN1)$, where T represents culture duration (hours), and N_1 and N_2 denote initial and final cell counts.

Cost-Effectiveness analysis

A GMP-based cost–effectiveness model was established to evaluate the economic feasibility of each tissue source. Components included consumables, enzymes, disposables, labor, cryostorage, and sterility assurance. All reagents were GMP-certified and obtained from Thermo Fisher, Gibco, Sigma-Aldrich, and Corning. Technician labor was calculated at USD 6.40/hour, with an average processing duration of 4 h per batch. Cryostorage was included at USD 0.09/mL/day, per institutional rates. All costs were normalized per 10^6 viable MSCs and adjusted for yield, contamination rate, and process duration (Supplementary Table S2).

Statistical analysis

All data analyses were conducted using IBM SPSS Statistics version 26.0 (IBM Corp., USA). The normality of continuous variables was evaluated using the Shapiro–Wilk test. Group differences were analyzed with the Kruskal–Wallis test, and pairwise comparisons were adjusted with Bonferroni-corrected Mann–Whitney U tests where appropriate. To determine independent predictors of MSC yield and contamination rate, a multivariate linear regression model was applied, controlling for maternal age, gestational age, and processing time. Regression coefficients (β), confidence intervals (95% CI), and p-values were reported for each variable. Data are expressed as mean ± standard deviation (SD) unless otherwise stated. A p-value < 0.05 was considered statistically significant.

Results

A total of 160 perinatal tissue samples—including amniotic fluid, amniotic membrane, umbilical cord, placental fragments, and whole placenta—were collected and processed under GMP-compliant conditions (Supplementary Table S1). Analyses focused on MSC yield, sterility outcomes, and GMP-adjusted cost efficiency per tissue type.

Quantitative analysis revealed significant variation in MSC yield among tissue sources ($p < 0.001$). Umbilical cord–derived MSCs exhibited the highest mean yield ($6.5 \times 10^6 \pm 0.8$ cells/sample), followed by amniotic fluid ($5.8 \times 10^6 \pm 0.6$) and amniotic membrane ($4.4 \times 10^6 \pm 0.5$). In contrast, whole placenta ($3.1 \times 10^6 \pm 0.4$) and placental fragments ($2.9 \times 10^6 \pm 0.3$) yielded significantly fewer viable MSCs ($p < 0.001$ vs. UC and AF; Bonferroni-corrected) (Fig. 1).

All cultures displayed typical spindle-shaped fibroblast morphology, plastic adherence, and reached 80–90% confluence within 6–8 days of initial seeding. Population doubling time (PDT) was significantly shortest in umbilical cord (28.3 ± 3.4 h) and longest in placental fragments (42.7 ± 4.8 h), indicating superior proliferative potential in cord- and fluid-derived MSCs (Supplementary Table S3).

Significant differences in microbial contamination were observed between tissue types ($p = 0.002$). Amniotic fluid exhibited the lowest contamination rate (3 ± 0.9%), followed by umbilical cord (6 ± 1.2%) and amniotic membrane (12 ± 2.4%). In contrast, placental fragments (21 ± 3.0%) and whole placenta (18 ± 2.7%) presented the highest contamination levels, likely due to prolonged exposure to the birth canal and maternal blood (Fig. 2).

A detailed cost breakdown indicated that amniotic fluid was the most economical tissue to process, with an average total cost of $26.80 ± 1.9 per sample, followed by umbilical cord (USD 59.24 ± 2.6). The umbilical cord

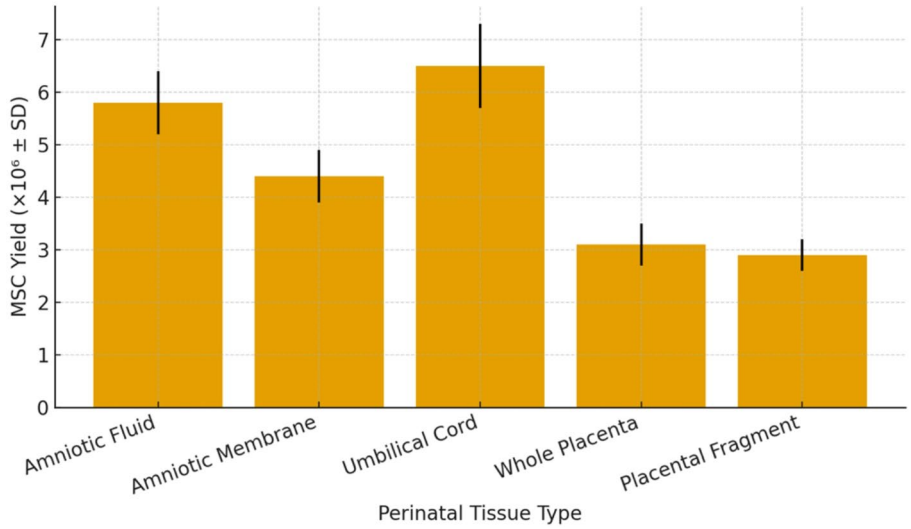

Fig. 1. Mean MSC yield (×10⁶ ± SD) across perinatal tissue types.

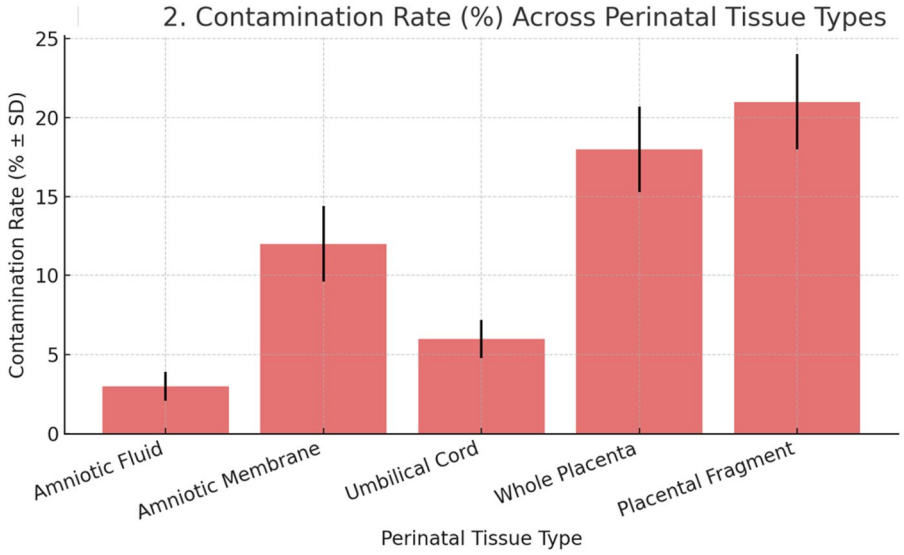

Fig. 2. Contamination rate (%) with standard deviation across perinatal tissue types.

followed closely ($59.24 ± 2.6), whereas whole placenta ($70.27 ± 3.2) and placental fragments ($66.22 ± 2.9) represented the least cost-efficient sources due to higher enzyme and reagent consumption. Amniotic membrane processing costs averaged $60.19 ± 2.8 per sample. When cost per 10^6 viable MSCs was normalized, umbilical cord and amniotic fluid demonstrated the most favorable yield-to-cost ratios, providing the best balance between production feasibility and sterility (Table 1; Fig. 3).

To identify independent predictors of MSC yield and contamination rate, multivariate linear regression analyses were performed, controlling for maternal age, gestational age, and processing time. The results indicated that tissue type remained the strongest independent predictor of MSC yield ($\beta = 0.61$, $p < 0.001$), followed by processing time ($\beta = -0.28$, $p = 0.04$), suggesting that longer intervals between delivery and processing slightly reduced viable cell recovery. Maternal and gestational parameters were not significant predictors ($p > 0.05$) (Table 2).

Comparisons among tissue types showed significant variation in MSC yield ($p < 0.001$), contamination rate ($p = 0.002$), and total cost per sample ($p < 0.001$). Post hoc analyses with Bonferroni correction confirmed that umbilical cord and amniotic fluid outperformed placental tissues in yield-per-cost efficiency ($p < 0.05$), whereas no significant difference was observed between the umbilical cord and amniotic fluid for either total cost ($p = 0.12$) or sterility-adjusted viability ($p = 0.16$) (Table 3).

Tissue Type	Procurement (USD)	Transport & Storage (USD)	Isolation (USD)	Total Cost (USD ± SD)	MSC Yield (×10⁶ ± SD)	Contamination Rate (%)
Amniotic Fluid	0.07	0.17	26.56	26.80 ± 1.9	5.8 ± 0.6	3 ± 0.9
Amniotic Membrane	0.33	0.17	59.69	60.19 ± 2.8	4.4 ± 0.5	12 ± 2.4
Umbilical Cord	0.33	0.18	58.73	59.24 ± 2.6	6.5 ± 0.8	6 ± 1.2
Placental Fragment	0.33	0.18	65.71	66.22 ± 2.9	2.9 ± 0.3	21 ± 3.0
Whole Placenta	2.05	0.18	68.04	70.27 ± 3.2	3.1 ± 0.4	18 ± 2.7

Table 1. Comparative costs, yields, and contamination rates of perinatal tissues. Kruskal–Wallis test.

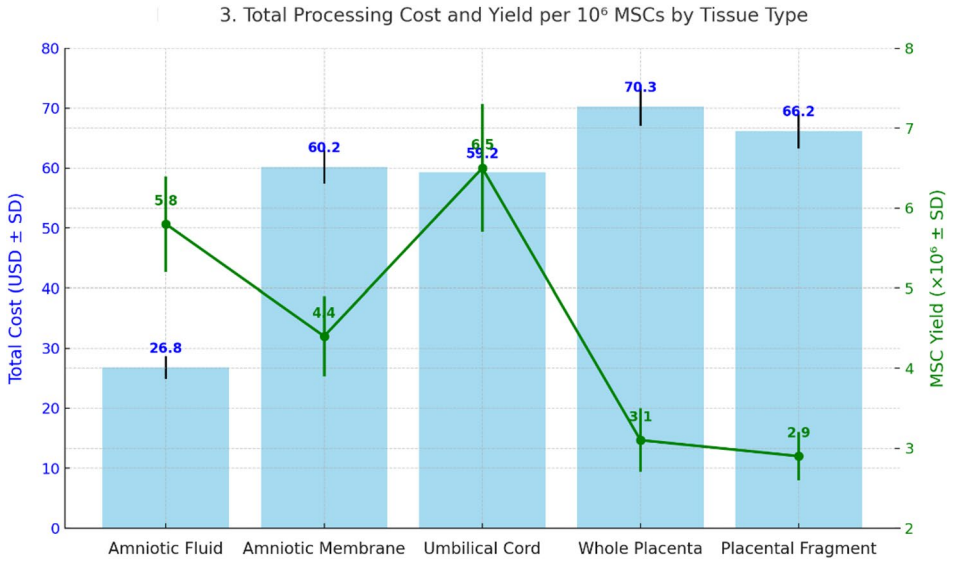

Fig. 3. Total processing cost and yield per 10^6 MSCs by tissue type.

Variable	β Coefficient	Standard Error	95% CI	*p*
Tissue Type	**0.61**	0.09	0.43–0.77	**< 0.001**
Processing Time (min)	**−0.28**	0.11	−0.52 – −0.04	**0.040**
Maternal Age (years)	0.07	0.08	−0.09–0.23	0.324
Gestational Week	0.05	0.07	−0.11–0.21	0.465

Table 2. Multivariate linear regression for predictors of MSC yield. Multivariate Linear Regression.

Parameter	Kruskal–Wallis χ^2 (df = 4)	*p*	Bonferroni-adjusted Post Hoc Comparisons	Significant Pairwise Differences
MSC Yield (×10⁶)	52.43	< 0.001***	UC > PL, PF; AF > PL, PF	UC, AF > PL, PF ($p < 0.05$)
Contamination Rate (%)	16.21	0.002**	AF < PL, PF; UC < PL, PF	AF, UC < PL, PF ($p < 0.05$)
Total Cost (USD)	49.77	< 0.001***	PL, PF > UC, AF; AM ≈ UC	PL, PF > UC, AF ($p < 0.05$)
Yield/Cost Efficiency	—	—	UC ≈ AF > PL, PF	UC, AF > PL, PF ($p < 0.05$)
Sterility-adjusted Viability	—	—	UC ≈ AF ($p = 0.16$)	No significant difference ($p > 0.05$)

Table 3. Comparative statistical analysis of MSC yield, contamination rate, and total cost across perinatal tissues. UC: Umbilical Cord; AF: Amniotic Fluid; AM: Amniotic Membrane; PL: Whole Placenta; PF: Placental Fragment.

Discussion

Perinatal tissues have emerged as a compelling source of MSCs owing to their high proliferative capacity, low immunogenicity, non-invasive procurement, and absence of substantial ethical concerns. However, meaningful clinical translation depends on more than biological potential alone; sterility, economic feasibility, reproducibility under GMP conditions, and scalability are equally decisive parameters for therapeutic application. Therefore,

multi-dimensional comparative analyses are necessary to determine which perinatal tissue types are best suited not only for research use but also for clinical biobanking and commercial-scale manufacturing.

Across evaluated tissues—amniotic fluid, amniotic membrane, umbilical cord, and placental tissues—umbilical cord consistently demonstrated the most favorable balance of yield, viability, proliferation, and manageable contamination risk. This aligns with previously described characteristics of Wharton's jelly as a proteoglycan- and hyaluronan-rich extracellular matrix environment, providing mechanical support and niche-like protection that preserves stemness features[16,17]. Umbilical cord–derived MSCs exhibited the highest viable cell counts and shortest population doubling times, indicating superior proliferative dynamics. These quantitative advantages, combined with minimally invasive postnatal retrieval, render the umbilical cord a strong candidate for standardized, GMP-compliant MSC banking.

Amniotic fluid–derived MSCs presented a moderately lower yield but achieved the lowest contamination rates and the lowest per-sample cost of GMP processing. These characteristics reflect the anatomically protected nature of amniotic fluid during cesarean section and the relatively simple processing workflow that does not rely on extensive enzymatic digestion. Previous reports by In 't Anker et al.[18] and recent neural regeneration studies[19] have underscored the therapeutic potential of AF-MSCs due to their embryonic-like gene expression profiles and high migratory capacity. When normalized to cost-per-viable cell, amniotic fluid and umbilical cord demonstrated comparable efficiency, making both tissues advantageous depending on clinical, logistical, or economic priorities.

Placental tissues presented a markedly different profile. Whole placenta and placental fragments showed the lowest viable MSC yields and the highest contamination risks. These findings correspond with prior analyses reporting that placental tissues, especially from vaginal deliveries, possess increased microbial load due to their direct exposure to maternal blood, vaginal flora, and delivery-related manipulation[20,21]. In addition, placental tissue processing requires prolonged enzymatic digestion, large reagent volumes, and considerable technical labor. Such factors escalate cost and increase variability, particularly in open-system GMP workflows. Nevertheless, placental MSCs remain biologically relevant due to their angiogenic and pro-regenerative secretome, including high expression of vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF)[21]. Optimization through closed-unit processing or automated bioreactor technologies may be necessary to harness this potential under clinical standards.

Cost-effectiveness analysis added a crucial translational dimension to this comparison. Amniotic fluid was identified as the most economical source on a per-sample basis due to minimal enzymatic processing and reduced sterility costs. However, umbilical cord provided the most optimal yield-to-cost ratio when normalized per 10^6 cells. These findings support existing economic simulations suggesting that umbilical cord MSCs could attain cost parity with bone marrow–derived MSCs in allogeneic manufacturing systems[22], especially when long-term expansion potential and lower senescence rates are considered[23]. In contrast, placental tissues imposed the highest total cost due to increased enzyme consumption, contamination control measures, and lower final cell output.

Sterility represents an indispensable criterion for GMP-grade MSC production. Amniotic fluid demonstrated the lowest pre-expansion contamination rate, while placental samples exhibited rates exceeding 18–21%. This discrepancy emphasizes the influence of tissue exposure, handling time, and sampling environment on sterility outcomes. Importantly, no contamination was detected after expansion, suggesting that the quality control pipeline—reducing processing time, implementing RBC lysis when necessary, and employing BACTEC™ microbial screening—successfully mitigated initial contamination risk.

Scalability further differentiates perinatal sources in terms of clinical applicability. Umbilical cord MSCs have been shown to maintain genomic stability, telomerase activity, and differentiation capacity during large-scale culture and 3D bioreactor expansion[23]. Conversely, enzymatic digestion procedures required for placental MSCs are time-intensive, technician-dependent, and difficult to automate. This reduces suitability for high-volume, closed-system manufacturing.

Several methodological and translational limitations warrant consideration. Most collected tissues originated from elective cesarean sections, limiting the ability to generalize findings to vaginal or emergent deliveries. The economic model applied reflects laboratory-scale GMP production and excludes downstream cost-of-goods elements such as sterility release testing, viral screening, regulatory documentation, batch certification, or distribution logistics. Additionally, long-term cryopreservation stability, post-thaw viability, senescence kinetics, extracellular vesicle secretion, and genomic integrity were not systematically analyzed, representing essential endpoints for future longitudinal research.

Despite these constraints, the present comparison provides a comprehensive framework integrating biological data, GMP sterility outputs, and real-cost parameters. Unlike earlier studies that focused exclusively on either phenotypic characterization or proliferation metrics, these results bridge the gap between laboratory feasibility and clinical-grade manufacturing readiness. The inclusion of multivariate regression strengthens inference by demonstrating that tissue type and processing time independently influence yield, regardless of maternal or gestational variables.

Further integration of molecular, epigenetic, and functional assays—combined with closed-system bioprocessing, digital batch tracking, and cost-of-goods sold (COGS) modeling—would advance the standardization of perinatal stem cell biobanking. Such efforts are essential for establishing regulatory consensus, optimizing large-scale production, and ensuring clinical accessibility.

Overall, umbilical cord and amniotic fluid demonstrate a favorable equilibrium of yield, sterility, proliferation, logistical feasibility, and economic viability. Placental tissues remain biologically valuable but currently present greater challenges under GMP constraints. Perinatal medical waste, when processed using structured, tissue-specific protocols, holds significant potential as a sustainable resource for regenerative medicine, allogeneic cell therapy, and future biomanufacturing platforms.

Conclusion

This study demonstrates that perinatal tissues differ significantly in their feasibility for GMP-compliant MSC production. Umbilical cord tissue showed the most favorable combination of viable cell yield, sterility, and processing cost. Amniotic fluid offered the lowest contamination risk and lowest cost, although with a comparatively lower cell yield. Placental tissues, despite their biological potential, were associated with higher contamination rates, reduced yield, and greater processing effort, making them less practical under current open-system GMP conditions.

These results emphasize the importance of tissue-specific procurement and standardized processing strategies in perinatal MSC banking. As this analysis reflects laboratory-scale GMP production, further research incorporating closed-system bioprocessing, large-scale cost modelling, cryopreservation outcomes, and functional post-thaw performance is needed to fully define clinical applicability. Properly optimized, perinatal medical waste remains a promising and sustainable source for regenerative medicine.

Implications for future research

The findings underscore the importance of developing scalable and standardized approaches for perinatal MSC biobanking. Future investigations may benefit from evaluating the functional comparability of MSCs derived from different perinatal tissues using harmonized immunophenotyping, trilineage differentiation assays, and high-throughput molecular profiling techniques. In addition, systematic assessment of senescence-associated markers, telomerase activity, genomic stability, and epigenetic modifications during extended culture would contribute to determining suitability for clinical-grade manufacturing.

Further optimization of tissue-specific isolation protocols—particularly for placenta-derived samples—could help reduce contamination risk and reliance on prolonged enzymatic digestion. The implementation of closed-system, automated processing platforms has the potential to improve sterility assurance and reproducibility, including in resource-limited settings.

Large-scale, multicenter cost-effectiveness analyses integrating clinical outcomes, regulatory requirements, and long-term storage logistics are also warranted. Incorporating ethical, legal, and governance frameworks—such as donor consent, cross-border cell banking, and data protection—will be essential to ensure safe, equitable, and sustainable translation of perinatal MSCs into regenerative therapies.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Received: 28 August 2025; Accepted: 11 December 2025
Published online: 15 December 2025

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Author contributions

Mehmet Çopuroğlu: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. Ömer Tarık Yalçın: Resources, Writing – review & editing, Supervision. Süleyman Gökhan Kara: Formal analysis, Validation, Writing – review & editing, Visualization.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

This study was approved by the Eskişehir Osmangazi University Clinical Research Ethics Committee (Approval No: 28; Date: August 3, 2023). Written informed consent was obtained from all participants prior to sample collection, in accordance with the Declaration of Helsinki.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-32738-9.

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