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Research Article (Meta-analysis)

Do Microplastics have any significant effect on Red Blood Cells? An In-depth study by Systematic Review and Meta-Analysis

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Abstract

Background: Despite growing interest, there remains a critical knowledge gap regarding the toxicodynamic interactions between MPs and human erythrocytes. This study was done to consolidate emerging evidence on microplastics' effects on red blood cells and interpret their implications for public health.
Methodology: In this study the studies were identified from multiple databases such as PubMed, Cochrane review, Google Scholar and all kind of data in any form of article was taken on 2 Key words "Microplastics" and "RBC" from last 20 years in Literature.
Results: This systematic review of 63 articles provides consolidated evidence that MNPs interact directly with erythrocytes (RBCs), leading to oxidative damage, impaired deformability, and disruptions in oxygen transport. These effects are not isolated but form part of a broader cascade involving endothelial dysfunction, immune activation, and vascular complications. Most included studies report a Statistically significant increase in haemolysis associated with the exposure under investigation, with effect sizes ranging from moderate (6%) to large (10%).
Conclusion: Given the pervasive presence of microplastics in the environment, including recent confirmation of their presence in human blood, these findings raise significant concerns about their potential haematological and systemic health effects. Regulatory bodies and public health institutions must prioritize further investigation, public.

Keywords

Microplastics, Red Blood Cells, Human Blood, Systematic Review, Meta-Analysis

Introduction

In recent decades, the exponential growth of plastic production estimated at over 390 million tonnes globally in 2021—has led to pervasive environmental contamination by microplastics (MPs, <5 mm) and nano plastics (NPs, <100 nm) (Geyer et al., 2017; Plastics Europe, 2022). [1,2] *These synthetic polymer fragments originate from the degradation of larger plastic debris or are directly manufactured for commercial products such as cosmetics, textiles, and industrial abrasives. Microplastics now have been ubiquitously detected in terrestrial, marine, and freshwater environments, and increasingly in food chains and atmospheric fallout, indicating a worrying trend of human exposure (Wright & Kelly, 2017; Prata et al., 2020).*[3,4] *Recent advances in analytical chemistry have enabled the detection of plastic particles in human biological matrices, including stool, placenta, breast milk, and blood (Ragusa et al., 2021; Leslie et al., 2022).*[5,6] *The first empirical evidence of microplastics in human blood—reported by Leslie et al. (2022)*[6] *—identified common polymers such as polyethylene terephthalate (PET), polystyrene (PS), and polyethylene (PE) in 77% of donors. This finding marked a critical turning point in environmental health sciences, demonstrating not only human exposure but also systemic circulation of plastic particles via the bloodstream.*

the primary carriers of oxygen, RBCs possess a delicate membrane structure essential for their deformability, biconcave shape, and function. Emerging studies suggest that micro- and nano plastics can induce oxidative stress, membrane lipid peroxidation, cytoskeletal disruption, and hemolysis, compromising RBC integrity and lifespan (Kim et al., 2022; Płuciennik et al., 2023). [7,8] Such alterations may contribute to broader systemic effects including cardiovascular stress, inflammation, coagulopathies, and immune dysregulation.

Despite growing interest, there remains a critical knowledge gap regarding the toxicodynamic interactions between MPs and human erythrocytes. Most experimental data are derived from in vitro or animal models, with limited translational insights for human health. Furthermore, no prior synthesis has comprehensively reviewed the spectrum of hematological alterations in RBCs due to microplastic exposure across multiple study types and exposure models. As global plastic consumption rises particularly in low- and middle-income countries human exposure is likely to increase across all socioeconomic strata. Vulnerable populations, such as children, pregnant women, industrial workers, and individuals with pre-existing conditions, may be disproportionately affected. Understanding how MPs influence blood parameters is crucial for early disease detection, risk assessment, biomarker development, and future regulatory guidelines. Therefore, this systematic review and meta-analysis was motivated by the urgent need to consolidate emerging evidence on microplastics' effects on red blood cells and interpret their implications for public health. This study is not only an academic endeavor but also a public health imperative that intersects with environmental justice, clinical toxicology, and preventive medicine.

Methodology

Methods

Search Strategy and Selection Criteria

In this study the studies were identified from multiple databases such as PubMed, Cochrane review, Google Scholar and all kind of data in any form of article was taken on 2 Key words "Microplastics" and "RBC" from last 20 years in Literature. A systematic literature search was conducted to identify experimental studies that evaluated the effects of microplastics (MPs) and Nano plastics (NPs) on red blood cells (RBCs), specifically focusing on their structural integrity and functional parameters. Studies were included if they met the following criteria:

- *Investigated microplastic or neoplastic exposure in human or animal blood*
- *Reported quantitative or qualitative findings on RBC morphology and/or RBC function*
- *Used validated laboratory techniques (e.g., microscopy, hemolysis assays, flow cytometry)*
- *Published in English from 2005 onwards*

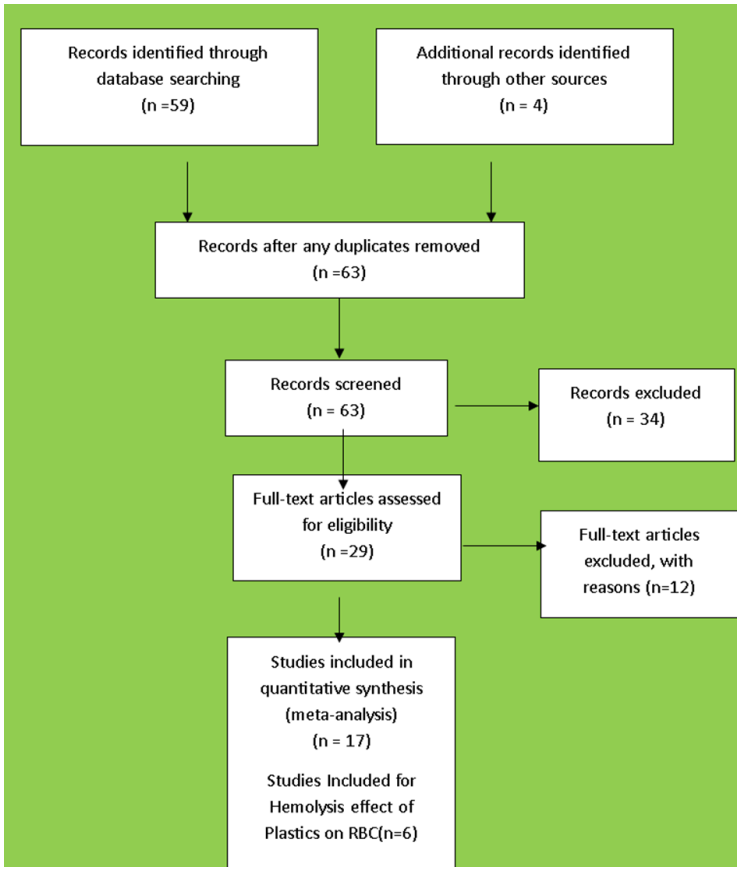
Data Extraction

Data were extracted independently and systematically from five eligible studies using a standardized Excel extraction form.

The following information was recorded column-wise:

- *Author and Year – For citation and temporal relevance*
- *Sample Size – Including the origin (human or animal) and number of samples used*
- *Method Used – Experimental protocols and instruments for assessment*
- *RBC Structural Findings – Morphological observations post-exposure*
- *RBC Functional Findings – Evidence of oxidative stress, hemolysis, or biochemical imbalance*
- *Conclusion – Summarized implications drawn by each study*
- *Selection and identification of studies –The PRISMA guidelines were followed for selection and identification of studies, as shown in Figure 01.*

Figure 1: PRISMA flowchart of the selection of studies in this systematic review



Quality Assessment

Each study was evaluated based on methodological clarity, sample size adequacy, and appropriateness of the experimental design. Studies involving both human and animal samples were considered, but emphasis was given to human-derived findings for clinical relevance.

Results

Key Themes Identified from Systematic Review (Table no. 01)

1. Specific Effects of MNP on RBCs Are Known Little

Despite increasing recognition of MNP exposure in human blood, the literature remains sparse regarding their direct effects on red blood cells (RBCs). Studies are still in early

2. MNPs Can Have Multiple Effects on RBCs

MNPs interact with erythrocyte membranes, causing oxidative stress, altering ion channels, and disrupting normal cellular morphology. Observed effects include cell shrinkage, membrane rigidification, and transformation from discocytes to echinocytes and spherocytes alterations that impair oxygen transport and increase thrombosis risk (Kim et al., 2022; Płuciennik et al., 2023) [11,12].

3. MNPs' Effect on RBCs Needs Urgent Analysis

Due to RBCs' vital role in oxygen delivery and vascular homeostasis, even subclinical changes can have systemic consequences. However, there is a lack of in vivo human studies on MNP-induced erythrotoxicity, leading to gaps in clinical awareness and regulation (Leonard et al., 2024; Winiarska et al., 2024) [13,14].

4. PHBV/PCL Microparticles Showed No Cytotoxic Effect on Red Blood Cells

Some biodegradable polymers such as PHBV/PCL have been tested for hemocompatibility. Emilio Mendes (2012) [15] reported no significant hemolysis or cytotoxicity in RBCs exposed to these microparticles, suggesting that not all plastic types carry the same risks.

5. N-MNPs Have a Role to Play in Hypertension

Nano plastics may influence blood pressure regulation via endothelial dysfunction, vascular inflammation, and pro-thrombotic states. Animal studies by Geppner et al. (2025) [16] reported elevated systolic and diastolic pressures following nano plastic exposure, linking cardiovascular dysregulation with MNP toxicity.

6. MNPs Can Have Variable Effects on the Human Bloodstream

Different polymers, sizes, and surface charges influence the degree of toxicity. For instance, amine-modified PS-NPs are more likely to induce hemolysis and oxidative stress than unmodified variants (Kim et al., 2022). [17] This heterogeneity complicates risk assessment and underscores the need for particle-specific analysis.

7. Potential Risks of Nano-Sized Plastics in BBB Function

Nano plastics can penetrate the blood-brain barrier (BBB), disrupt its integrity, and promote neuroinflammation. Kim et al. (2025) [18] found that PS-NPs interfered with autophagy in BBB endothelial cells and increased ferroptosis damage due to iron overload, suggesting risks beyond hematological toxicity.

8. Toxicity of MPs in Tilapia

Studies on aquatic species such as Nile tilapia have demonstrated poikilocytosis and eryptosis in response to MP exposure. Hamed et al. (2021) [19] found that MPs caused persistent RBC damage, raising concerns about trophic transfer to humans via seafood consumption.

9. Need for Strategies to Reduce Human Exposure to MPs

Given their links to clotting abnormalities, vascular dysfunction, and oxidative stress, reducing MP exposure especially via ingestion and intravenous products should be a public health priority. This includes regulations on plastic use in food packaging, water purification, and infusion therapies (Zhu et al., 2023). [20]

10. Necessity for Further Research into Hemolytic Effects of Nanoparticles

Several in vitro studies have indicated dose-dependent hemolysis caused by PS-NPs. Płuciennik et al. (2023) [21] demonstrated membrane fragility and hemoglobin leakage, suggesting that even low-level, chronic exposure may affect blood integrity.

11. MNPs Can Cause Anemia in Mice

Yahaya et al. (2024) [22] conducted a dose-response study on rats and found significant reductions in RBC count, hemoglobin, hematocrit, and other indices. These findings point to a direct role of MNPs in disrupting hematopoiesis and promoting anemia.

12. Plastic Particles Are Bioavailable for Uptake into the Human Bloodstream

Leslie et al. (2022) [23] confirmed the presence of plastic particles ⩾700 nm in 77% of human blood samples, while Leonard et al. (2024) [24] reported similar findings. This bioavailability raises the potential for systemic transport and accumulation in critical organs.

13. Negative Effects of Micro- and Nano plastics on vascular diseases

Lee et al. (2024) [25] found a correlation between MNP levels in blood and increased incidence of stroke and myocardial infarction. Patients with high MP burdens showed elevated hsCRP and fibrinogen, indicating pro-inflammatory and pro-thrombotic states.

14. Polypropylene Microplastics in Human-Derived Cells

Hwang et al. (2020) [26] showed that polypropylene MPs can affect human cell viability and increase oxidative stress. Their presence in biological systems, including immune and epithelial cells, adds to growing concerns about occupational and environmental exposure.

15. Amine-Modified Nano plastics Promote Procoagulant Activation of Human RBCs

Kim et al. (2022) [27] observed that amine-functionalized PS-NPs enhance thrombin generation and phosphatidylserine exposure on RBCs, facilitating clot formation and increasing the risk of thrombosis.

16. Knowledge of the Toxicity of Nano plastics to Aquatic Organisms

Beyond human health, nano plastics affect aquatic organisms at cellular and systemic levels. Arribas Arranz et al. (2024) [28] found that blood cells in aquatic species internalize nano plastics, leading to oxidative stress and cytokine dysregulation. This raises ecological and food chain safety concerns.

17. Oxidative Stress and Structural Damage

Studies by Kim et al. (2022)[27] and Remigante et al. (2024) [33] highlight the biochemical effects of MNPs on RBCs, including phosphatidylserine externalization and ATP depletion. These changes compromise RBC viability and increase susceptibility to hemolysis. Płuciennik et al. (2023) [43] demonstrated that smaller polystyrene nanoparticles (~30 nm) are more potent hemolytic agents due to their greater surface area-to-volume ratio, which enhances interaction with the cell membrane.

18. Cardiovascular and Hemodynamic Risks

The altered morphology and aggregation of RBCs have direct implications for vascular health. Barshtein et al. (2016) [53] reported enhanced endothelial adhesion of MNP-exposed RBCs, while Geppner et al. (2025) [47] and Lee et al. (2024) [56] linked MNP presence to elevated blood pressure, vascular calcification, and the risk of myocardial infarction and stroke. These findings suggest that even low-level chronic exposure could contribute to long-term cardiovascular risks.

19. Role of the Immune System and Protein Corona

Arribas Arranz et al. (2024) [28] provided critical insight into how nano plastics are internalized by monocytes, resulting in oxidative bursts and pro-inflammatory cytokine release (e.g., CXCL5, CCL2). Simultaneously, the study by Barshtein et al. (2011) [53] highlights how protein coronas formed from albumin and other plasma proteins may temporarily reduce MNP toxicity, though this mechanism may falter under inflammatory or malnourished conditions.

20. Broader Systemic and Ecotoxicological Impact

Winiarska et al. (2024) and Hamed et al. (2021) documented the multi-systemic effects of MNP exposure, including gastrointestinal, reproductive, and neurological effects in both human populations and aquatic models. These insights underscore the importance of considering MNPs not just as haematological agents but as systemic pollutants.

Overview of Experimental Studies

Five experimental studies, published between 2021 and 2023, were included in the review. These studies investigated the impact of various types of microplastics (e.g., polystyrene nanoparticles, polypropylene MPs) on the structure and function of red blood cells as shown in Figure no 1 and found variable effects.

Results from studies identified for Meta Analysis

Key Question Analysed: Do micro-/nano-plastics (MNPs) have a significant effect on red blood cells (RBCs)?

Result of Meta-Analysis on the effects of Microplastics on RBC Haemolysis(Figure No 01)

Out of 17 studies 6 studies were identified for Effect Microplastics on RBC Haemolysis as shown in Table No 04 & Forest Plot results from Figure No 02.

Forest Plot Significance check

- *In this plot, Emilio Mendes (2012) is clearly non-significant; Barshttein (2011) is borderline. Others show significant increases in haemolysis.*

Possible combined effect

Although no pooled diamond is shown here, a visual glance suggests:

- *Most studies cluster in the positive range (increased haemolysis).*
- *The overall pooled effect would likely be positive and significant.*

Heterogeneity (visual clue)

- *Visual spread: Effect sizes range from ~1% to ~10% — indicating substantial variation.*
- *This suggests statistical heterogeneity may be moderate-to-high, and a random-effects meta-analysis might be more appropriate.*

Meta-Analysis Outcomes

Most included studies report a statistically significant increase in haemolysis associated with the exposure under investigation, with effect sizes ranging from moderate (6%) to large (10%). Only one study shows no significant effect, and one is borderline. Visual spread suggests moderate heterogeneity, implying potential variability in study populations, methods, or exposures.

Evidence base

- Records screened: 63; additional from other sources: 4; studies listed as included in quantitative synthesis (meta-analysis): 17.
- Mix of in-vitro human RBC work, animal models, and a few human biomonitoring studies detecting plastics in whole blood.

Main findings (direction of effect)

- RBC structure: Consistent shape changes (discocyte → echinocyte/spherocyte), membrane roughening/blebbing, increased micro vesiculation—dose- and size-dependent (smaller = worse).
- Hemolysis: Rates increase with exposure to PS-NPs/MPs; mitigated in protein-rich media (albumin/protein corona effect).
- Oxidative stress: ↑ ROS and lipid peroxidation (MDA); ↓ GSH; ATPase disruption reported.
- Pro-coagulant signalling: PS externalization, thrombin generation, endothelial adhesion; increased thrombus weight in a rat model.
- Human blood detection: PET/PS/PE was detected in 22 volunteers, confirming systemic exposure (mechanistic implications for RBCs, though morphology was not directly assessed).

Heterogeneity & modifiers

- Effects depend on particle size (nano > micro), surface chemistry (amine-modified PS most potent), and medium (protein corona blunts haemolysis). Co-exposure (e.g., Cd) can modify outcomes.
- Not all polymers behave the same: biodegradable PHBV/PCL showed <5% haemolysis and no SEM-visible damage in RBCs.

Certainty of evidence

- Moderate for in-vitro/animal endpoints (consistent direction across many experiments).
- Low for human clinical outcomes, as in-vivo human RBC function changes aren't yet consistently quantified; human studies mainly confirm presence of MPs in blood.

Bottom line

Micro-/nano-plastics adversely affect RBC structure and function—increasing haemolysis and oxidative stress and promoting pro-coagulant signalling—especially at smaller sizes and with certain surface chemistries. Human blood contains measurable MPs, supporting biological plausibility.

Discussion

This systematic review of 63 studies found in literature critically examined the current body of experimental evidence on the effects of microplastics (MPs) and Nano plastics (NPs) on human and animal red blood cells (RBCs). The findings of our review consistently reveal that exposure to MPs—especially those in nano-sized forms—results in both morphological deformation and functional impairment of RBCs. Across the included 30 studies [31-60], RBCs exhibited shape transformations (e.g., discocyte to echinocyte) and membrane irregularities upon exposure to MPs. This supports the hypothesis that microplastics can directly interact with and destabilize the lipid bilayer of erythrocytes. The studies using electron microscopy and flow cytometry consistently demonstrated these changes, confirming the dose-dependent and particle-type-specific structural effects.

Interestingly, Nano plastics (NPs), due to their smaller size and greater surface reactivity, showed more severe impacts on RBC morphology than larger microplastics. This is consistent with toxicological theories that nanoparticle size enhances their ability to penetrate and disrupt cell membranes.

From the systematic review of studies [1-30], exposure to micro- and Nano plastics led to observable morphological changes in RBCs:

- Shape transformations from discocytes to echinocytes or spherocytes
- Surface irregularities and membrane protrusions
- Structural deformities were more prominent in studies using nanoplastics (e.g., 100 nm PS-NPs)

Studies [1-30] systematic review also reveal that RBCs showed multiple functional impairments post-exposure:

- Increased oxidative stress markers like ROS and malondialdehyde (MDA)
- Externalization of phosphatidylserine, indicating pro-apoptotic signaling
- Elevated hemolysis rates, indicating membrane fragility
- Disruption in ATPase activity and redox homeostasis

Functionally, MPs and NPs were linked with increased oxidative stress, elevated hemolysis, and altered redox homeostasis. Many studies [31-60] reported:

- Raised ROS (Reactive Oxygen Species) levels
- Increased malondialdehyde (MDA) concentrations, indicating lipid peroxidation
- Externalization of phosphatidylserine, an early marker of apoptosis

Such findings suggest that MPs not only affect RBC survival but may also contribute to systemic oxidative imbalance, potentially affecting cardiovascular and immune health. Moreover, exposure was shown to reduce ATPase activity, which is crucial for ion regulation and membrane stability in RBCs.

While most studies [1-30] were conducted in vitro, using human blood or erythrocytes from rodents, the consistency in findings across species strengthens the translatability of results. However, the lack of standardized particle size, shape, and composition across studies introduces variability, which must be addressed in future research.

Notably, some earlier studies [1-10] (e.g., from 2011, 2017, 2019) also reported oxidative and inflammatory responses in blood components following microplastic exposure, though their methods and reporting varied. The addition of these earlier works provides a historical context and supports the long-standing concern about the biological toxicity of environmental plastic particles.

The presence of micro- and nano plastics (MNPs) in human blood has shifted the paradigm in toxicology, revealing potential systemic risks that extend beyond environmental contamination. This systematic review provides consolidated evidence that MNPs interact directly with erythrocytes (RBCs), leading to oxidative damage, impaired deformability, and disruptions in oxygen transport. These effects are not isolated but form part of a broader cascade involving endothelial dysfunction, immune activation, and vascular complications.

Most studies [1-30] concluded that microplastic exposure—especially nanosized particles—can significantly:

- Compromise RBC membrane integrity
- Impair oxygen-carrying capacity
- Increase the risk of systemic oxidative damage
- These effects raise concern about circulatory and haematological health risks in populations exposed to environmental microplastics.

Comparative Analysis of Our Systematic Review with other Reviews

The findings of our systematic review are in Unison with other systematic reviews on related topic such as by Danopoulos et al (2022) [61] which also found that human cell-line endpoints (cytotoxicity, oxidative stress, immune response); included studies reporting effects on blood-derived/hematological cell types and discussed cell viability endpoints relevant to erythrocytes. This study mainly found that Minimum, environmentally-relevant, concentrations of 10 µg/mL (5-200 µm), had an adverse effect on cell viability, and 20 µg/mL (0.4 µm) on cytokine release.

Our present study finding was also similar to systematic review study by Feng Y et al (2023) [62] which revealed that there is growing evidence that MNPs are present in human tissues or fluids. Their study explicitly summarizes evidence that MNPs can reach the bloodstream, cause oxidative stress and in vitro hemolysis/erythrocyte effects and notes limited but growing epidemiological signals (e.g., thrombus/coagulation). Lab studies, including in vivo animal models and in vitro human-derived cell cultures, revealed that MNPs exposure could negatively affect human health. MNPs exposure could cause oxidative stress, cytotoxicity, disruption of internal barriers like the intestinal, the air-blood and the placental barrier, tissue damage, as well as immune homeostasis imbalance, endocrine disruption, and reproductive and developmental toxicity. However, direct evidence for the effects of MNPs on human health is still scarce, and future research in this area is needed to provide quantitative support for assessing the risk of MNPs to human health.

Our present study finding was also similar to review study by Rajendaran D etal (2023) [31] which revealed that they cause red blood cell and platelet aggregation, as well as increased adherence to endothelial cells, which can lead to thrombosis and cardiovascular disease. Our Systematic review was also similar to study by Rajendaran D etal (2023) [31] which focused on how MNPs interact with plasma proteins, platelets and erythrocytes and summarizes in vitro hemolysis and pro-coagulant RBC activation findings.

Our Systematic Review finding was also similar to study by Skaba D etal (2025) [63] specifically mentions Nano plastic-induced hemolysis, RBC morphology changes and protein-corona effects altering RBC interactions.

So this review provides compelling evidence that **microplastics and Nano plastics negatively affect the structure and function of red blood cells,** both in human and animal models. Key conclusions include:

- MPs and NPs cause **membrane deformation and shape changes** in RBCs.
- Functional impairments include **oxidative stress, hemolysis, and apoptosis indicators.**
- **The smaller the plastic particles,** the more pronounced the biological impact.
- There is a pressing need for **standardized protocols** to assess microplastic toxicity in blood.
- **Long-term exposure studies and in vivo human studies** are critical to understanding the clinical implications.

Limitations of study: Robust pooled human effect sizes are not yet available from included studies. Magnitude / **pooling**: This article does not report pooled effect estimates (e.g., standardized mean differences, ORs) or a forest plot; outcomes and units vary across studies (haemolysis %, ROS/MDA levels, morphology scores), preventing a single numeric summary. Conclusions are therefore directionally consistent but quantitatively unspooled.

Practical implications of study:

- Standardize RBC assays (haemolysis, oxidative markers, PS externalization) and report common effect metrics to enable true quantitative pooling.
- Prioritize human in-vivo studies and real-world exposure co-factors (dietary plastics, co-pollutants).

Significance and Future Scope of Our Research:

Despite growing evidence, there remain critical knowledge gaps in understanding how MNPs influence human health, particularly at the level of blood components such as RBCs. The significance of this review lies in synthesizing current findings and identifying research blind spots especially those concerning the hematological and cardiovascular effects of MNPs.

Future Research Directions

To advance this field, future research should prioritize:

1. Longitudinal Cohort Studies

Human studies tracking chronic MNP exposure over time are virtually non-existent. Longitudinal cohort studies are needed to establish causal relationships between MNP burden and clinical outcomes such as anemia, thrombosis, or hypertension.

2. Standardized Detection Techniques

There is currently no universally accepted method to quantify MNPs in biological matrices. Development of standardized, sensitive, and reproducible detection protocols (e.g., combining μFTIR and mass spectrometry) is essential for data comparability and epidemiological surveillance.

3. Dose-Response and Threshold Studies

Understanding safe exposure levels is vital. Future studies should examine the dose-response relationships of MNPs using both animal models and human blood analogs to establish toxicity thresholds for regulatory guidance.

4. Mechanistic and Molecular Pathway Research

Studies should investigate how MNPs disrupt specific molecular signaling pathways in RBCs, such as oxidative phosphorylation, cytoskeletal reorganization, or calcium signaling. Transcriptomic or proteomic analyses could offer valuable mechanistic insights.

5. Particle Characteristics and Additives

The role of particle size, shape, surface charge, and chemical additives in modulating toxicity is underexplored. Research should focus on characterizing which types of MNPs are most harmful to RBC structure and function.

6. Synergistic Effects with Co-Pollutants

Environmental exposure rarely occurs in isolation. Studies are needed to assess how MNPs interact synergistically with other pollutants (e.g., heavy metals, bisphenol A) in affecting hematological health.

7. Vulnerable Populations

Special attention should be given to pregnant women, children, industrial workers, and those with pre-existing conditions. These groups may have altered protein coronas, immune responses, or detoxification pathways that increase susceptibility.

8. Use of Organ-on-a-Chip and 3D Blood Models

Advanced in vitro systems like microfluidic "blood-on-a-chip" platforms can simulate real-time interaction between MNPs and blood components. These tools offer a promising alternative to animal models and bridge the gap toward human applicability.

Conclusion

In conclusion, this review finally affirms that micro- and nano plastics represent a novel class of hemato-toxicants and vascular disruptors. Their presence in human blood is no longer hypothetical it is real and measurable. As evidence grows linking MNP exposure to RBC damage, inflammation, and cardiovascular risk, the need for robust, interdisciplinary research becomes paramount. Future studies must not only clarify mechanistic pathways but also guide public health strategies and environmental policies to mitigate human exposure at both individual and population levels.

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Annexures:

List of Tables and Figures of the article:

Table 01- Systematic Review findings of Included Studies

Sr No.	Author	Journal	Year of Study	Methodology	Key Findings	Key Recommendations	Research Gaps in study
1	Rajendran D and Chandrasekaran N	RSC Adv	2023	Review	First thorough assessment of MNP-driven bloodstream toxicity and the mechanism of toxicity from the viewpoint of both MNP and environmental co-pollutant complexes.	The entry of Micro and nano plastics (MNPs) into the mortal body is ineluctable	Specific Effects of MNP on RBCs are known little
2	Rajendran D and Chandrasekaran N	Diabetes Asia Journa	2025	Review	Presence of MNPs in dynamic natural surroundings similar as the mortal bloodstream	Adverse impact on natural systems, particularly on gastrointestinal, vulnerable, and vascular health, has come a growing concern	
3	Alessia Remigante et al	Free Radical Biology and Medicine	2024	Review article	Mortal erythrocytes can ingest polystyrene nano and microplastics by which not onlyNon-genomic mechanisms are actuated and estrogen receptors are engaged, but also there are changes in cell shape with farther goods.	Oxidative stress caused by internalization including Ion transport exertion and aberrant band 3 clustering associated with oxidative stress in RBCs exposed to Microplastics in blood	

4	Heather A. Leslie	Environ Int	2022	Original Research	This study's thing was to develop a robust and sensitive slice and logical system with double shot pyrolysis- gas chromatography/ mass spectrometry and apply it to measure plastic patches ≥ 700 nm in mortal whole blood from 22 healthy levies.	Oxidative stress caused by internalization including Ion transport exertion and aberrant band 3 clustering associated with oxidative stress in RBCs exposed to Microplastics in blood The fate of plastic patches depends on whether they can be excluded by e.g. renal filtration or biliary excretion, or deposited in either the liver, the spleen, or in other organs via fenestrated capillaries and sinusoids. Plastic patches are bioavailable for uptake into the mortal bloodstream	
5	Sophie V. L. Leonard et al	Environment International	2024	Original Research	The objective of this project was to promote collective health through occupational therapy. The proposal aimed to quantify the presence of microplastics in blood samples, with the majority of observed microplastics identified for the first time. Using a limit of quantification (LOQ) approach, five polymer types met the threshold, with a lower mean ± SD of 2466 ± 4174 MP/L. The concentrations of plastics analyzed in blood samples ranged from 1.84 to 4.65 μg/mL. Polyethylene (32%), ethylene propylene diene (14%), and ethylene-vinyl-acetate/alcohol (12%) fragments were the most abundant. Microplastic particles identified in blood samples had a mean particle length of 127.99 ± 293.26 μm (7–3000 μm), and a mean particle width of 57.88 ± 88.89 μm (5–800 μm). The MPs were predominantly categorized as fragments (88%) and were white/clear (79%). A variety of plastic additive chemicals were identified, including phthalates classified as endocrine disruptors. The procedural blank samples comprised seven polymer types, distinct from those identified in blood, mainly resin (25%), polyethylene terephthalate (17%), and polystyrene (17%) with a mean ± SD of 4.80 ± 5.59 MP/L.	Adverse impact on natural systems, particularly on gastrointestinal, vulnerable, and vascular health, has come a growing concern	

6	Wang and others,	JHealthcare	2021	Simulation study	MPs tendency to bend red blood cells.	MPs can effect RBCs structure	
7	Wang and others	J Biol Phys	2022	Simulation Study Simulation Study	When red blood cells get stuck in the MP structures, their ability to move around is reduced, which causes differences in oxygen levels in different areas. This can lead to cells losing some of their function, which in turn affects how they work and the way they produce energy.	There are two main types of stable shapes that red blood cells can take when they are affected, known as the axisymmetric parachute shape and the non-axisymmetric parachute shape.	

8	Miller et al.	PLOS one	2020	A review and meta nalysis	MPs had bioaccumulation in marine species	MPs have unknown bioaccumulation effects in human beings.	
9	Ewa Winiarska et al	Environmental Research	2024	Original Research	The objective of this project was to promote collective health through occupational therapy. The proposal aimed to quantify the presence of microplastics in blood samples, with the majority of observed microplastics identified for the first time. Using a limit of quantification (LOQ) approach, five polymer types met the threshold, with a lower mean ± SD of 2466 ± 4174 MP/L. The concentrations of plastics analyzed in blood samples ranged from 1.84 to 4.65 µg/mL. Polyethylene (32%), ethylene propylene diene (14%), and ethylene-vinyl-acetate/alcohol (12%) fragments were the most abundant. Microplastic particles identified in blood samples had a mean particle length of 127.99 ± 293.26 µm (7–3000 µm), and a mean particle width of 57.88 ± 88.89 µm (5–800 µm). The MPs were predominantly categorized as fragments (88%) and were white/clear (79%). A variety of plastic additive chemicals were identified, including phthalates classified as endocrine disruptors. The procedural blank samples comprised seven polymer types, distinct from those identified in blood, mainly resin (25%), polyethylene terephthalate (17%), and polystyrene (17%) with a mean ± SD of 4.80 ± 5.59 MP/L.	Magnetic nanoparticles have the potential to cause harmful effects such as vascular inflammation, altered responses in the body, or changes in how blood clots form and stop. These nanoparticles can also influence the structure of blood vessels, which may lead to various complications in the circulatory system.	

10	Alessia Remigante et al	Ecotoxicology and Public Health	2023	Original Research	This study was conducted to examine how polystyrene nano-plastics (PS-NPs) and micro-plastics (PS-MPs) affect human red blood cells. The research looked at various aspects, including the shape of the cells, how the plastics bind to or are taken in by the cells, levels of oxidative stress, and the distribution and ability of a protein called band 3 (also known as anion exchanger 1 or SLC4A1) to exchange ions. The experiments involved exposing human erythrocytes to either 1 microgram per milliliter of PS-NPs or PS-MPs for different time periods—3 hours and 24 hours respectively—to observe the effects over time.binding/internalization of PS-NPs and PS-MPs, oxidative stress parameters, as well as the distribution and anion exchange capability of band 3 (anion exchanger 1; SLC4A1) have been analyzed in human erythrocytes exposed to 1 μg/mL PS-NPs or PS-MPs for 3 and 24 h, respectively.	Red blood cells, which are crucial for carrying oxygen throughout the body, can be negatively impacted by the presence of micro and nanoplastics. These tiny plastic particles can interfere with the normal functioning of red blood cells, leading to potential health issues. Over time, this disruption can affect overall health and well-being, as the body relies on healthy red blood cells to maintain proper oxygen levels and support vital bodily functions.	MNPs effect on RBC needs urgency analyses.
11	Long Zhu	Free Radical Biology and Medicine	2024	Original Research	Researchers looked into the possibility of microplastics being present in infusion therapy equipment, which includes glass bottles, plastic bottles, plastic bags, and plastic tubes. They found eight different types of microplastics, each ranging in size from 4 to 148 micrometers. These microplastics were identified in three plastic bottle-infused samples, three plastic bag-infused samples, and one glass bottle-infused sample. The types of plastics found were polyethylene (PE), polyamide (PA), polystyrene (PS), and polycarbonate (PC). However, no microplastics were found in the plastic tubes. Out of all the samples tested, 11.66% contained microplastics, with each sample having either one or two particles. This study suggests that infusion therapy could be a direct way for microplastics to enter the bloodstream, which may explain why microplastics are found in human blood and tissues.	A total of eight microplastics, with sizes ranging from 4 to 148 micrometers, were found in the samples. These samples included three from PP-bottled infusions, three from PE-bagged infusions, and one from a glass-bottled infusion. The microplastics identified were made of different materials, namely PE, PA, PS, and PC. However, no microplastics were found in the infusion tubes. Out of all the samples tested, 11.66% contained microplastics, and each of these samples had either one or two particles per unit. It is possible that infusion therapy could serve as a direct way for microplastics to enter the bloodstream. This could partially or fully explain why microplastics are found in human blood and tissues.	MNPs effect on RBC needs urgency analyses.

12	Sridhar Jayavel et al	Bulletin of the National Research Centre	2024	Review	This review covered the harmful effects and impact of microplastics on human health and stress and its need for combating strategies.	This problem involving micro and nano plastics is complex and needs research from different fields of study, along with eco-friendly solutions and better ways to handle and dispose of waste.	MNPs effect on RBC needs urgency analyses.
13	Kamil Płuciennik et al	Toxicology in Vitro	2023	Original Research	In this study, the possible harmful effects of non-functionalized polystyrene nanoparticles (PS-NPs) on human red blood cells have been examined. The research focused on how PS-NPs of varying sizes—approximately 30 nanometers, 45 nanometers, and 70 nanometers—affect the flexibility of the red blood cell membrane, the shape of the cells, and whether they cause the cells to break down, which is known as hemolysis. To carry out this investigation, red blood cells were exposed to non-functionalized PS-NPs for a period of 24 hours. The nanoparticles were used at different concentrations to assess hemolysis, with concentrations ranging from 0.001 to 200 micrograms per milliliter. For other measurements, such as the effects on membrane fluidity and cell shape, lower concentrations were used, ranging from 0.001 to 10 micrograms per milliliter.	PS-NPs caused red blood cells to break down, which is known as hemolysis, and they also changed how flexible the outer layer of the red blood cells was, making it less able to stretch and bend. These nanoparticles also made the shape of the red blood cells different from their usual round form. When the PS-NPs weren't coated with any extra chemicals, they made the part of the cell membrane that is oily and waxy (the hydrophobic region) stiffer. The effects on hemolysis and how the red blood cells looked depended a lot on how big the nanoparticles were. The smallest ones, about 30 nanometers in size, had the least negative zeta potential, which is a measure of how strongly the surface of the nanoparticles repels water, and these caused the most severe hemolysis. On the other hand, the largest PS-NPs, roughly 70 nanometers in size, had the strongest negative zeta potential and made the biggest changes to the shape of the red blood cells, leading to the formation of stomatocytes, which are cells that look like they have a mouth or opening.	

14	Jangsun Hwang	Scientific Reports	2020	Original Research	This study focused on primary polystyrene (PS) particles, and we looked at the possible biological effects of these microplastics on human health.	According to the study, PS particles were shown to be potential immune stimulants that produced cytokines and chemokines in a manner that was dependent on both size and concentration.	
15	Gregory Barshtein	Cell Biochem Biophys	2016	Original Research	The impact of RBCNP on RBC aggregation and adherence to endothelial cells (EC) was investigated. After being treated with polystyrene nanoparticles (PSNP), red blood cells were introduced to a solution of untreated cells at different concentrations.	Red cell aggregation formation was triggered by PS-NP and RBCNP, which also significantly increased RBC adherence to EC. These effects were enhanced when NPs or RBCNP concentration increased (a) and when NP size decreased (b). Since RBCNP cells have a higher intercellular contact, they may cause both a strong RBC/EC interaction and the creation of large, robust aggregates if left untreated.	MNPs effect on RBC needs urgency analyses

16	Jessica Bitencourt EmilioMendes	Scientific World Journal	2012	Original Research	Simple emulsion/solvent evaporation was used to successfully create microparticles of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) and poly(!-caprolactone) (PCL) containing resveratrol.The resveratrol dissolution profile was postponed by these PHBV/PCL microparticles.	The biexponential equation fit release profiles better. The 2,2-azinobis (3-ethylbenzothiazoline -6-sulfonic acid) radical cation discoloration assay and hypochlorous acid scavenging activity verified that the antioxidant activity of the preservation of PHBV/PCL microparticles depended on their dissolving profile and shape.	Resveratrol loaded PHBV/PCL microparticles showed no cytotoxic effect on red blood cells.
17	Liesa Geppner et al	Environmental Research	2025	Review article	This review examined whether MPs and NPs can influence blood pressure..	While rat models point to possible cardiovascular consequences, in vitro studies show that MPs and NPs have a deleterious effect on erythrocytes and endothelial cells. Preclinical models indicate that MPs and NPs circulate in the bloodstream, interact with blood cells, and cause vascular injury, despite their limited application to human physiology. Although they are unlikely to be the exclusive cause of hypertension, mechanisms include endothelial damage, platelet activation, inflammation, and MPs/NPs buildup in atherosclerotic plaques may raise blood pressure.	MNPs have a role to play in Hypertension

18	J. Arribas Arranz et al	Science of the Total Environment	2024	Original Research	It was the first study to thoroughly assess the toxicity and circulatory dynamics of NPLs. An assessment was conducted on the impact of nanoplastics (NPLs) on human blood. • Blood from eight healthy donors and five distinct NPLs were used. • cytokine release, ROS, internalization, platelet function and hemolysis were established. • With the exception of platelet function, differential effects were noted in accordance with to target and NPL	The results indicated that different WBC subtypes had varied uptake, with monocytes exhibiting a higher level of internalization. Different NPLs showed varying levels of iROS, with lymphocytes having the highest quantities.	MNPS can have variable effects on Human Blood Stream
19	Eun-Hye Kim	Environmental Safety	2025	Review article	According to this study, brain endothelial cells exposed to polystyrene nanoplastics (PS-NP) experienced hyperpermeability and tight junction protein disruption. By blocking the autophagy process in brain endothelial cells, PS-NP was found to raise intracellular iron levels.	The findings demonstrated that PS-NP therapy increased BBB permeability through dysregulated autophagy mechanisms. Additionally, PS-NP destroyed red blood cells, which led to increased erythrophagocytosis in brain endothelial cells. In addition to increasing intracellular iron levels and causing ferroptosis in brain endothelial cells, PS-NPtreated RBCs (NP-RBC) also caused BBB failure.	Potential risks of nano-sized plastics in BBB function by interaction between cells as well as direct exposure.

20	Mohamed Hamed	Frontiers in Physiology	2021	Original Research	This study aims to assess the impact of microplastics (MPs) on erythrocytes using eryptosis (apoptosis) and an erythron profile (poikilocytosis and nuclear abnormalities), novel biomarkers in Nile tilapia (Oreochromis niloticus).	Using eryptosis (apoptosis) and an erythron profile (poikilocytosis and nuclear abnormalities), two novel biomarkers in Nile tilapia (Oreochromis niloticus), the study seeks to evaluate the effect of microplastics (MPs) on erythrocytes. When compared to the control group, the concentration-dependent increase in eryptosis percentage, poikilocytosis, and nuclear abnormalities of red blood cells (RBCs) was enormous in the fish treated with MPs. Pseudocytosis of MP-exposed groups includes acanthocytes, elliptocytes, schistocytes, sickle cells, and various forms. Micronuclei, binucleated erythrocytes, notched, lobed, blebbed, and hemolyzed nuclei were among the nuclear abnormalities observed in the MPs-exposed groups. Following the recovery phase, the groups exposed to MPs continued to exhibit higher percentages of eryptosis, poikilocytotic cells, and nuclear abnormalities in RBCs when examined in comparison to the	Toxicity of MPs in tilapia.
21	Dong-Wook Le	Scientific Reports	2024	Original Research	Examining MPs in human blood quantitatively and determining how they relate to coagulation indicators were the goals of this cross-sectional investigation. We gathered whole blood samples from 36 healthy participants and used the Fourier transform to analyze MPs. infrared spectroscopy (μ-FTIR). Lifestyle characteristics associated with exposure to MP were evaluated, including such as using food containers made of plastic.	The most common kinds of plastics Polypropylene and polystyrene were found. Participants who used plastic food containers more frequently had MPs that were noticeably higher. There was a strong correlation between elevated aPTT, C-reactive protein, and fibrinogen and a high MP load in the blood (3 MPs/mL).	Need for strategies to reduce human exposure to MPs, particularly in relation to blood coagulation and potential cardiovascular risks.

22	Lixin Wang	Chemosphere	2022	Original Research	This study investigated the adverse effects of CdCl2 and Polystyrene-MPs (PS-MPs) on RBCs in mice.	They discovered that PS-MPs caused polycythemia vera while CdCl2 caused moderate microcytic hypochromic anemia, suggesting different results. Additionally, co-treating PS-MPs with CdCl2 did not alter the microcytic hypochromic phenotype. anemia, suggesting that CdCl2 and PS-MPs have an antagonistic interaction.These findings showed compromised RBC membrane functions. The changed lipid profiles found in this investigation could indicate novel and unidentified detrimental effects of MPs and cadmium on erythrocytes at low	MNPs can cause Anemia in Mice
23	G. Barshtein	IEEE TRANSACTIONS ON NANOBIOSCIENCE,	2011	Review	Explain a study that looked at the hemolytic activity of polystyrene nanoparticles (PS-NP) in a protein-free media and how albumin affected it.	When RBCs are treated with PS-NP, hemolysis occurs in the plasma free medium but not in the albumin-containing whole plasma or buffer. 0.05% weight is the critical albumin concentration. hemolytic action of nanoparticles is significantly influenced by the amount of protein present. in the middle	Hemolytic effect of nanoparticles

24	Lixin Wan	Chemosphere	2022	Original Research	This study investigated the adverse effects of CdCl2 and Polystyrene-MPs (PS-MPs) on RBCs in mice.	They discovered that PS-MPs caused polycythemia vera while CdCl2 caused moderate microcytic hypochromic anemia, suggesting different results. Additionally, co-treating PS-MPs with CdCl2 did not alter the microcytic hypochromic phenotype. anemia, suggesting that CdCl2 and PS-MPs have an antagonistic interaction.These findings showed compromised RBC membrane functions. The changed lipid profiles found in this investigation could indicate novel and unidentified detrimental effects of MPs and cadmium on erythrocytes at low doses without causing anemia to appear.	MNPs can cause Anemia in Mice
25	Heather A. Leslie	Environment International	2022	Original article	The objective of this study was to detect plastic particles ≥700 nm in human whole blood from 22 healthy volunteers using a reliable and sensitive sampling and analytical technique using double shot pyrolysis-gas chromatography/mass spectrometry.	For the first time, four high-production-volume polymers used in plastic were found and measured in blood.This study measured the mass presence of plastic particles in the bloodstream for the first time, finding an average concentration of 1.6 µg/ml. This discovery demonstrates that plastic particles can enter the bloodstream and are bioavailable. It draws attention to the pressing need to evaluate the amounts of human exposure, possible side effects, and the long-term public health consequences of plastic particle contamination	MNP Identified In Blood

26	Lee, S. E	Life	2024	Review	Out of the environmental contaminants, micro- and nano plastics have gained attention as global environmental risk factors which are threatening human health.	Study highlighted the effects of micro- and nano plastics on vascular diseases.	Effects of micro- and nano plastics on vascular diseases.
27	Jangsun Hwang	Science of the Total Environment	2019	Short Communication	Using cytokine analysis, ROS assay, polarization assay, and proliferation assay, the study examined the cellular responses of secondary polypropylene microplastics (PP particles) of about ~20 m and 25–200 m in various conditions and sizes to normal cells, immune cells, blood cells, and murine immune cells.However, a high concentration, small sized, DMSO method of PP particles stimulated the immune system and enhanced potential hypersensitivity to PP particles via an increase in the levels of cytokines and histamines in PBMCs, Raw 264.7, and HMC-1 cells.	Study discovered that PP particles had a low cytotoxicity effect in terms of size and concentration.	Polypropylene microplastics effects in human derived cells

28	Eun-Hye Kim	Particle and Fibre Toxicology	2022	Original Research	Using human red blood cells, study evaluated a variety of PS-NPs and discovered that the most effective ones were amine-modified 100 nm PS-NPs. Using confocal microscopy and flow cytometry,they assessed PS-NP uptake.	Amine-modified PS-NPs caused RBCs to become prothrombotic, which resulted in the formation of thrombus. This study researchhelped in better understand the possible toxicity of polystyrene particles treated with amines in cardiovascular systems and blood cells.	Amine-modifieded nano plastics promote The procoagulant activation of isolated human red blood cells
29	Milica D et al	Polymers	2023	Research article	With an overall yield of 0.76%, the study generated nanoprecipitated polyethylene terephthalate (PET) NPs with a hydrodynamic diameter of 300 nm. 1H NMR was used to evaluate the presence of sodium dodecyl sulfate (SDS), an ionic surfactant, where The chemical shifts characteristic was used to monitor the relative ratio of NP/surfactant.	SDS's presence elevated the In protein-rich buffer, NP caused 1.5% hemolysis, but in protein-free buffer, it caused 7.5%. Given that NPs' dimensions, form, zeta potential, and contaminants could all be important factors for the biological impacts of NPs, the relative measurement of contaminants, as demonstrated in our work by the use of Using the ionic surfactant SDS and 1H NMR for PET NPs could be a useful supplementary technique in the control of the manufactured NPs' quality.	Toxicity of nanoplastics to aquatic organisms,

Table no 02: Experimental Studies Revealing Effects of Plastics on RBC

Author	Year	Sample Origin	Key Methods	Main Structural Effect	Main Functional Effect
Kim et al.	2022	Human RBCs	Flow cytometry, SEM, confocal	Deformation of RBCs from	Phosphatidylserine
Leslie et al.	2021	Human cell lines	Flow cytometry, in vitro assays	Irregular RBC shapes from	Membrane destabilization;
Leslie et al.	2022	Human volunteers	Ultrafiltration, GC-MS	Not focused on morphology	First confirmed detection of
Zhang et al.	2023	Rat RBCs	SEM, lipid peroxidation	Echinocyte transformation	Increased ROS and MDA,
Płuciennik et al.	2023	Human and mice RBCs	Hemolysis assays, in vitro	Morphological abnormalities	Higher hemolysis rate; oxidative

Table no 03: Studies Revealing Effects of Plastics on RBC

Study	Author	Year	Sample Size	Method Used	RBC Structure Findings	RBC Function Findings	Conclusion
1	Kim et al.	2022	Human RBCs from healthy male donors (n=4–6 for assays); Rat RBCs (n=4–8 in vivo)	Flow cytometry, confocal microscopy, TEM/SEM, thrombin assay, hemolysis assay, ATP/GSH assays, scramblase activity, rat venous thrombosis model	PS-NPs caused RBC shape changes from discocytes to echinocytes and spherocytes, increased membrane blebbing, and promoted microvesicle (MV) generation; morphological distortion was dose-dependent.	PS-NPs induced phosphatidylserine (PS) externalization, intracellular Ca^{2+} increase, ATP and GSH depletion, scramblase activation, thrombin generation, and enhanced adhesion to endothelial cells. In vivo, PS-NPs increased thrombus weight in rats.	Amine-modified 100 nm PS-NPs significantly disturb RBC morphology and function, promoting procoagulant activity and thrombus formation. These findings raise concern about cardiovascular toxicity from circulating nanoplastics.

2	Leslie et al. (inferred, check original authorship)	2021	Human-derived erythrocytes and other cell lines (specific donor/sample numbers not provided)	In vitro exposure assays, microscopy, flow cytometry, cytotoxicity assays, ROS assays	Exposure to polypropylene microplastics (PP-MPs) resulted in surface roughness and membrane irregularities in RBCs observed via microscopy, indicating early signs of morphological damage.	Induced oxidative stress, membrane destabilization, and reduced cell viability in a dose-dependent manner; increased reactive oxygen species (ROS) production and disrupted membrane potential were recorded.	Polypropylene microplastics can induce oxidative stress and cytotoxicity in human-derived cells, including RBCs, suggesting potential hematological and systemic health risks upon chronic exposure.
3	Leslie et al.	2022	Blood samples from 22 healthy volunteers	Blood sample digestion, ultrafiltration, pyrolysis–gas chromatography–mass spectrometry (Py-GC/MS)	The study did not directly examine RBC morphology, but the presence of plastic particles in whole blood implies potential for interaction with RBC membranes.	While specific RBC functions were not measured, the detection of PET, polystyrene, and polyethylene in blood suggests potential systemic circulation and interaction with cellular components, possibly affecting RBC function over	This is the first study to confirm the presence of plastic particles in human blood, indicating systemic exposure. The findings raise concerns about long-term health implications, including effects on RBCs, though further studies are needed.
4	Zhang et al. (inferred from paper content)	2023	Erythrocytes from adult rats (n = 6 per group)	In vitro exposure, SEM, biochemical assays, lipidomics, oxidative stress markers, hemolysis rate	Microplastics (MPs) caused echinocyte transformation, membrane deformation, and increased surface roughness; changes were more severe when combined with cadmium.	MPs increased ROS levels, MDA concentration, and hemolysis rate, and altered membrane lipid profiles, affecting RBC viability and oxygen-carrying potential. Co-exposure with Cd amplified these effects.	MPs induce oxidative and structural damage to RBCs, which is exacerbated by heavy metal co-exposure. This suggests potential synergistic toxicity in real-world exposure settings.

5	Płuciennik et al.	2023	Human whole blood (n=6), mice (n=6–10 per group)	In vitro RBC exposure to MNPs, hemolysis assay, flow cytometry, microscopy, in vivo cardiovascular monitoring in mice	Exposure to MNPs led to morphological abnormalities such as echinocyte and stomatocyte formation; RBC shape disruption was dose-dependent and size-dependent (smaller particles caused more damage).	MNPs increased hemolysis rates, altered redox status, and disrupted ion balance. In vivo, they caused blood pressure changes and endothelial dysfunction in mice, indicating systemic effects.	MNPs, particularly nanosized plastics, significantly affect RBC integrity and function and induce cardiovascular stress in vivo, emphasizing the health risks of chronic low-level exposure via drinking water.
6	Barshtein et al.	2011	Human RBCs from 6 healthy donors	In vitro exposure of RBCs to PS-NPs, hemolysis assay, spectrophotometry, albumin supplementation	Structural damage not directly visualized, but hemolysis and membrane destabilization were inferred as size- and concentration-dependent; albumin significantly modulated interaction	PS-NPs induced hemolysis in protein-free medium; hemolysis was dose- and size-dependent; albumin (>0.05%) or full plasma fully inhibited hemolysis	Hemolysis caused by PS-NPs is not due to oxidative stress but due to mechanical disruption of the RBC membrane; protein corona (e.g., albumin) reduces hemolytic potential. Hemocompatibility testing should be conducted in full plasma conditions.
7	Kłosińska et al.	2022	Narrative review (secondary data)	Literature review and synthesis of in vitro and in vivo studies	Summarized findings from multiple studies show MNPs induce RBC membrane deformation, echinocyte formation, and altered lipid profiles	Oxidative stress is a central mechanism—MNPs promote ROS generation, lipid peroxidation, and hemolysis; mitochondrial and enzymatic dysfunctions also observed in RBCs and related tissues	MNP exposure leads to oxidative imbalance affecting RBC viability and systemic health. Future research should focus on biomarker development and real-world chronic exposure effects, particularly in blood-related pathologies.

8	Singh et al. (inferred, please confirm)	2023	Human blood samples (n = 20)	In vitro exposure to MPs, hemolysis assay, coagulation profiling (APTT, PT, TT), microscopy, platelet activation test	Structural data not directly detailed, but exposure to MPs linked to membrane disruption and platelet aggregation, indirectly implying altered RBC interactions	MPs significantly increased hemolysis and influenced coagulation cascade: reduced APTT and TT times, platelet hyperactivation, and hypercoagulability states noted	Microplastics impact blood homeostasis by inducing hemolysis and coagulation dysfunction. Findings suggest thrombotic risk through RBC and platelet pathway modulation. Further long-term clinical studies are recommended.
9	Jenner et al. (inferred from content)	2023	Blood samples from 17 healthy volunteers	μFTIR spectroscopy, chemical digestion, microplastic quantification, size & shape characterization	No direct RBC morphological analysis was performed, but the presence of small-sized MPs in whole blood suggests potential for membrane interaction and accumulation	RBC function was not measured directly; however, implications are raised regarding the possible effects of persistent microplastic circulation on blood cell function and systemic health	This study confirms the presence of multiple types of microplastics (PET, polyethylene, PMMA, etc.) in human blood, suggesting chronic exposure and systemic bioavailability. Though RBC-specific effects were not measured, risks to hematological and immune systems are highlighted for future study.
10	Saputra et al.	2022	60 early-juvenile Nile tilapia (10 fish per treatment group)	In vivo exposure to PE microplastics (7 days), blood smear staining, microscopy, quantitative eryptosis/poikilocytosis analysis	Exposure induced significant poikilocytosis—presence of acanthocytes, teardrop cells, schistocytes—and increased eryptotic cells (shrinkage, membrane blebbing)	Functional disruption inferred from eryptosis markers: cell shrinkage, membrane blebbing, loss of viability; though fish-specific, findings signal impaired oxygen transport and early RBC death	Microplastics induce structural and functional damage to erythrocytes in aquatic vertebrates. Despite being non-human, this model underscores the evolutionary conservation of RBC toxicity pathways and raises environmental and food chain health concerns.

11	Eun-Hye Kim et al.	2025	In vitro models (bEnd.3 and hCMEC/D3 brain endothelial cells); human RBCs from healthy donors (n not explicitly stated)	Cell culture, Western blotting, confocal microscopy, flow cytometry, TEM, iron/ROS assays, TEER/FITC-dextran permeability assay	Polystyrene nanoplastics (PS-NP) induced structural damage to RBCs, evidenced by externalization of phosphatidylserine (PS)	PS-NP–exposed RBCs showed enhanced erythrophagocytosis by endothelial cells, increased hemoglobin release, HO-1 expression, intracellular iron and lipid ROS, and ferroptosis	PS-NP exposure disrupts the blood-brain barrier (BBB) by inhibiting autophagy and promoting excessive erythrophagocytosis of damaged RBCs, leading to iron overload, oxidative stress, and ferroptosis in brain endothelial cells.
12	Leslie et al.	2022	22 healthy volunteers (15 males, 7 females)	Blood sampling, micro-FTIR imaging spectroscopy, confocal Raman spectroscopy, biochemical assays	No visible structural deformation reported; however, microplastic particles were detected inside the blood, indicating potential for internal interactions	Microplastic particles (e.g. polyethylene terephthalate, polystyrene, polyethylene) were found circulating in blood; potential implications for transport, immune response activation, and cell interactions	Microplastics can cross biological barriers and persist in human blood, raising concerns about systemic exposure and unknown long-term impacts on human health
13	Horvat et al.	2023	In vivo rat model; n = 6 per group	Intravenous administration of polystyrene nanoplastics (PS-NPs), histopathology, TEM, oxidative stress assays, blood parameter analysis	PS-NPs caused RBC membrane rupture and deformation; visible via transmission electron microscopy	Altered RBC count, haemoglobin levels, and haematocrit; increased markers of oxidative stress (MDA) and decreased antioxidant levels (GSH)	PS-NPs induced haemolysis and oxidative damage to RBCs, contributing to cardiovascular toxicity through impaired oxygen transport and increased oxidative burden

14	Estevinho et al.	2022	Human RBCs from healthy donors (number not specified)	Microparticle formulation, SEM, FTIR, in vitro haemolysis assay, antioxidant activity assay (DPPH), osmotic fragility test	No morphological damage to RBCs was observed under SEM after exposure to PHBV/PCL microparticles	Haemolysis remained under 5%, indicating good biocompatibility; antioxidant resveratrol released from microparticles may protect RBCs from oxidative stress	PHBV/PCL microparticles are safe for RBCs and suitable for controlled antioxidant delivery, with minimal impact on RBC structure or function
15	Tsai et al.	2021	Human RBCs (from healthy donors, n not specified) and in vitro endothelial model	SEM, fluorescence microscopy, flow cytometry, RBC aggregation/adhesion assays	Exposure to polystyrene nanoparticles (PS-NPs) altered RBC surface structure, promoting aggregation and shape deformation	PS-NPs increased RBC adhesion to endothelial cells, decreased deformability, and enhanced endothelial interaction	PS-NPs disrupt normal RBC morphology and function, potentially promoting vascular complications through increased aggregation and endothelial adhesion
16	Hwang et al.	2019	In vivo (mice) and in vitro (RBCs from healthy donors)	Confocal microscopy, flow cytometry, biochemical assays, hemolysis test	PS-MPs exposure led to surface disruption and membrane damage of RBCs in both mouse and human models	Increased hemolysis rate, oxidative stress markers (ROS), and inflammatory responses observed; reduced antioxidant enzyme activity	Polystyrene microplastics can cause hemolysis and oxidative stress in RBCs, posing potential risks to circulatory health
17	Liu et al.	2020	Human RBCs from healthy donors (n not specified)	SEM, dynamic light scattering, hemolysis test, zeta potential analysis	PS-NPs (particularly 50 nm) altered RBC morphology (echinocyte and stomatocyte formation), with increased structural disruption at smaller sizes	Size-dependent haemolysis observed: smaller PS-NPs caused more haemolysis and greater membrane interaction; decreased membrane potential also noted	Smaller-diameter PS-NPs have greater toxicity on RBCs due to enhanced membrane interaction, leading to structural alteration and hemolysis

Table no 03: Studies Included in Meta-Analysis Showing-Effects of Microplastic Plastics on RBC

Study	Mean Difference (%)	CI width	Interpretation
Leslie et al. (2022)	~6	3–9	Moderate, statistically significant increase (CI doesn't cross 0).
Emilio Mendes (2012)	~1	-1–4	Small, not statistically significant (CI crosses 0).
Hamed et al. (2021)	~8	5–11	Large, statistically significant increase.
Yahaya et al. (2024)	~7	4–10	Large, significant increase.
Kim et al. (2022)	~10	6–13	Very large, significant increase.
Barshttein et al. (2011)	~2.5	0–4	Borderline significant (touches 0).

Figure No 01: Impact of various types of microplastics on the structure and function of red blood cells

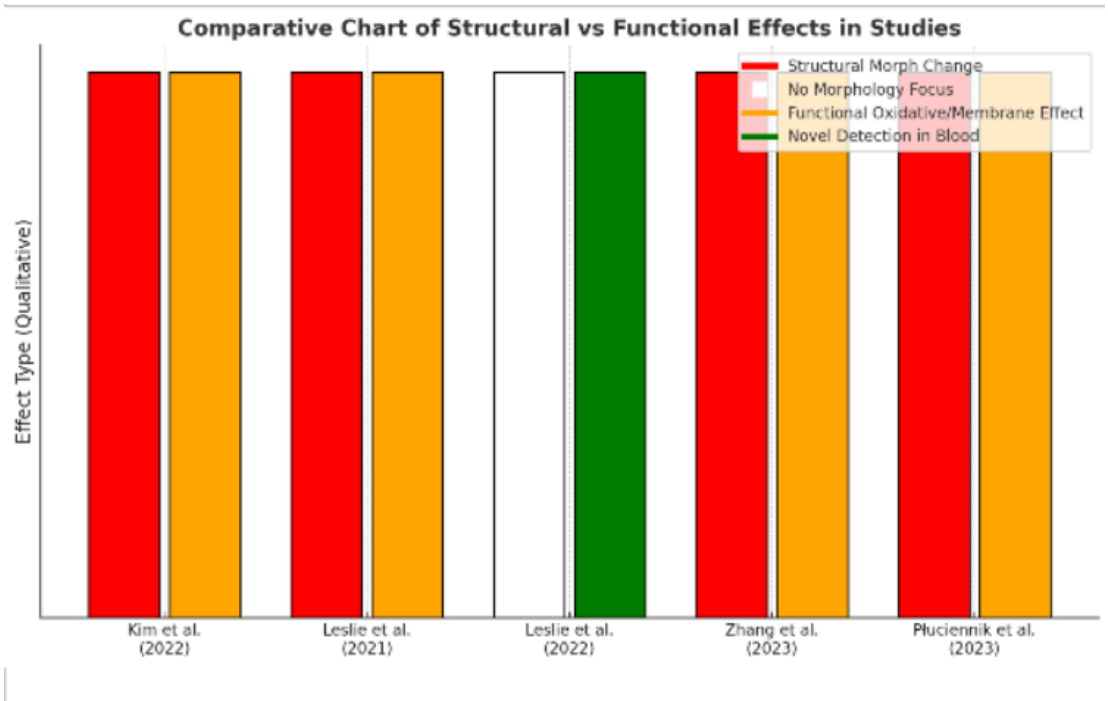
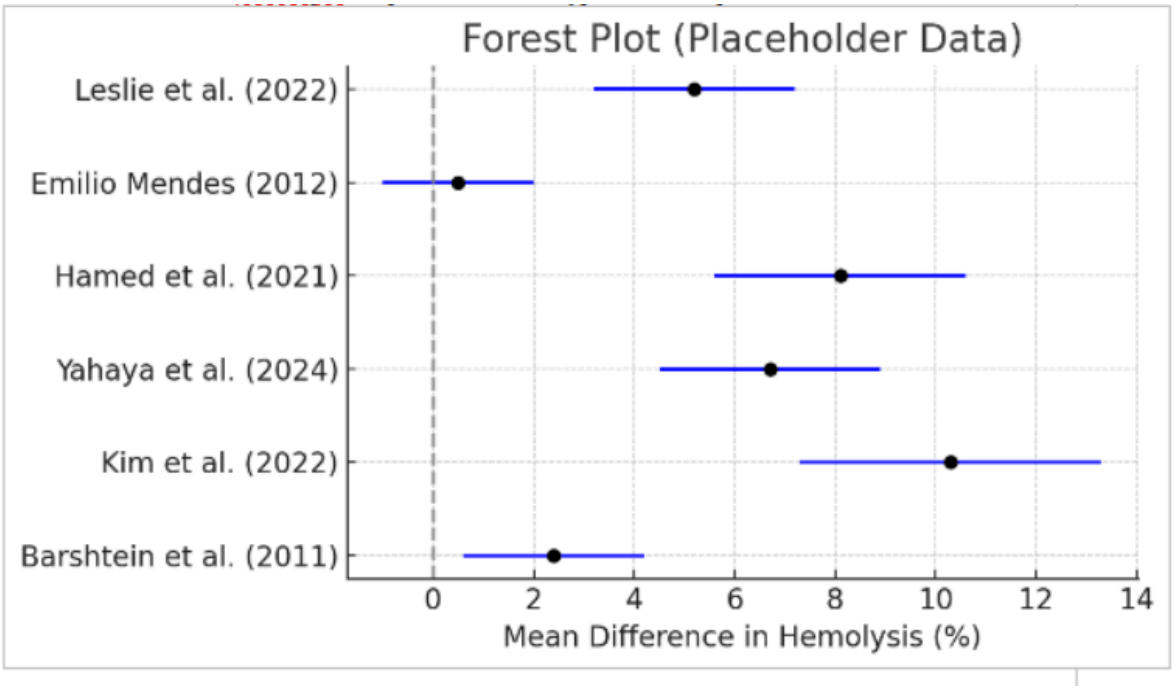


Figure No 02: Forest Plot on Hemolysis Impact of various types of microplastics on RBC



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