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A Retrospective, Multicenter, Observational Real World Post Market Clinical Follow Up Study to Evaluate Acute Safety and Device Procedural Success of ADVACRYL PLUS (Triclosan Coated Triclosan Coated Polyglactin 910) Surgical Suture. (ADVACRYL PLUS PMCF Study)

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Abstract

In this real-world experience Post-Marketing Clinical Follow-up study conducted in accordance with EU MDR 2017/745 in 103 subjects from >80 surgical centers across various surgical specialties, ADVACRYL PLUS (Triclosan Coated Polyglactin 910) braided, synthetic absorbable sterile surgical sutures demonstrated excellent suture, needle, and overall performance. No wound complications or adverse events were reported in this study during the follow-up period of 3 months, and there were no reports of prolonged or repeat hospitalization. ADVACRYL PLUS (Triclosan Coated Polyglactin 910) sutures are a safe and effective option for a very wide variety of surgical procedures in a diverse population.

Keywords: Triclosan Coated Polyglactin 910, braided, synthetic absorbable, Antibacterial suture.

INTRODUCTION

Sutures are sterile surgical threads used to approximate and/or ligate tissues. They are essential for wound closure in a variety of surgical procedures, including general surgery, gynecology, ophthalmology, and cardiovascular surgery. Sutures are available in a wide range of materials, including natural (e.g., catgut, silk) and synthetic (e.g., nylon, polyester, Polyglactin 910). [1]

Braided, synthetic absorbable sterile surgical sutures are a type of suture that is composed of multiple strands woven together. This braiding process results in a suture that is strong, flexible, and easy to handle. Synthetic absorbable sutures are made from a variety of materials. Advanced MedTech Solutions (AMS)

https://www.amsltd.com/products/advacryl-plus a braided coated synthetic absorbable suture called ADVACRYL PLUS that is composed of a copolymer made from 90% glycolide and 10% L-lactide, coated with a mixture composed of Poly (glycolide-co-lactide) and calcium stearate. Suture is coated with Triclosan, a broad-spectrum antibacterial agent.

ADVACRYL PLUS suture is available in both dyed and undyed form. ADVACRYL PLUS suture complies with United States Pharmacopeia requirement for "Absorbable Surgical Suture" and the European Pharmacopoeia for "Sterile Synthetic Absorbable Braided Sutures".

ADVACRYL PLUS Antibacterial sutures are intended for use in general soft tissue approximation and/or ligation, except for ophthalmic, cardiovascular and neurological tissues.

The absorption process begins at the suture surface and progresses inward. The progressive loss of tensile strength and eventual absorption of ADVACRYL PLUS occurs by means of hydrolysis where the copolymer degrades to glycolic and lactic acids which are subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength followed by a loss of mass. All the original tensile strength is lost between four- and five-weeks post implantation. Absorption of ADVACRYL PLUS suture is essentially complete up to 80 days. The rate of absorption depends on several factors, including the suture diameter, the type of tissue, and the patient's individual metabolism.

Suture construction	Suture Color	Tensile strength Retention (%)		Mass Absorption* (days)
Braided	Undyed / Violet	14 days	75%	Essentially complete up to 80 days
		21 days	40% - 55%	
		28 days	15%	

Mass Absorption: Time in days required for suture to be totally absorbed in the body.

ADVACRYL PLUS suture is designed to offer the following advantages.

Features	Benefits
Triclosan Coated Antibacterial Suture	Effective in reducing the risk of Surgical Site Infections
Tighter Braided Construction	Smoother suture surface for minimal tissue drag & trauma and Lesser chances of bacterial colonization.
Excellent Handling Characteristics	Superior first throw hold, easy knot-repositioning and excellent knot security & lesser knot slippage
Superior swage point integrity	Advanced tipping ensures minimal suture detachment at the swage point

Pharmacokinetic studies in animals and humans have shown that triclosan is rapidly absorbed, well distributed in the body, metabolized in the liver, and excreted by the kidneys, with no indication of accumulation over time.[2] Strength of Triclosan was 200-400 ppm and purity is 99.6%.

Triclosan passively dissipates from implanted sutures to the surrounding tissues where it is absorbed into the bloodstream and widely distributed, but not confined to any particular tissue or organ system. Triclosan is rapidly metabolised in the liver principally by Phase II metabolism to glucuronide and sulphate conjugates with an elimination half-life of 13 hours after a single oral exposure. Therefore, triclosan is cleared from the bloodstream (over 99%) in approximately 3·8 days. Conjugated triclosan is readily water-soluble and is excreted from the body by the kidneys. There is no evidence that triclosan accumulates in the body over time and this pharmacokinetic profile makes it suitable for clinical use.

There is no associated experimental chronic or major adverse target organ toxicity, carcinogenicity, or potential for mutagenic, clastogenic or teratogenic effects and no adverse effects on male or female fertility, or endocrine function. [2]

FDA (US) has approved polyglactin 910 sutures coated with triclosan for commercial use since 2002. There were eight reports in human use in the past ten years. Five studies favored antimicrobial suture, two studies showed no difference and one study against this new suture. The first report was published by Ford et al in 2005 show prospective, randomized, controlled, open-label, comparative, single-center study was conducted on 147 pediatric patients (age 1-18 years) undergoing various surgical procedures with either polyglactin 910 sutures coated with antibiotic triclosan or polyglactin sutures without triclosan. The endpoints of this study focused on intraoperative handling and wound healing characteristics instead of surgical site infection that the aim of this investigated suture. For intra-operative handlings were favorable and not significantly different for both sutures, although coated polyglactin 910 sutures with triclosan received more “excellent” scores (71% vs. 59%). Wound healing characteristics were comparable for both sutures, except significantly fewer patients with triclosan sutures reported pain on day one compared with patients without triclosan sutures (p=0.01). The overall incidence of adverse events was 18%; none was device related, and there was no difference between treatment groups. [3]

A Meta-analysis of 22 RCTs including 6642 patients concluded that at a risk of 138 SSIs per 1000 procedures, the use of Triclosan-coated sutures (TCS) reduced this by 39 (95 per cent CI 19, 55). Trial sequential analysis confirmed a RR reduction of 15 per cent for the use of TCS 23. [4]

Further, Reregistration Eligibility Decision (RED) Document for Triclosan states that in conclusion, even with the reliance of conservative assumptions in estimating risks to account for the considerable uncertainties in converting spot urine concentration to dose, the NHANES data as analyzed for triclosan sufficiently characterize the aggregate risks as meeting the definition of not resulting in unreasonable adverse effects [5]

According to the latest NICE Guidelines on Surgical Site Infections, the evidence overall favoured triclosan-coated sutures over standard sutures for reducing surgical site infection. The guidance committee therefore agreed that they should be considered as an option for wound closure in all types of surgery, and that their use in pediatric surgery should be emphasized in particular.

They further emphasized its cost effectiveness by noting that it is likely that the increased cost (of using Triclosan Coated sutures) will be outweighed by savings from a reduction in the number of surgical site infections, which are costly to treat. [6]

According to expert opinion, the use of translational models to study further the safety profile of Triclosan coated sutures is unavoidable, given that absorbable sutures cannot be removed from patients for research purposes. Exploring the triclosan bioavailability of triclosan on sutures in animal studies would be scientifically acceptable only if the protocol were accurately specified with in vitro study results, had a

significant benefit for patients, and was in compliance with animal ethics, compatible with 3Rs principles. [7]

ADVACRYL PLUS sutures have been used widely in various types of surgical procedures. We are not aware of any systematic study done till date in an Indian population to determine safety and performance of the Triclosan Coated Polyglactin 910 suture in real world scenario.

MATERIALS AND METHODS

Study Design and Conduct

A real-world experience study was designed as 'A Multicenter, Real World Retrospective Post Market Clinical Follow-up Study to Evaluate Acute Safety and Device Procedural Success of Triclosan Coated Polyglactin 910 (ADVACRYL PLUS) Surgical Suture.' (ADVACRYL PLUS PMCF STUDY)

A combination of heterogeneous data from different centers was collected to reinforce analyses and strengthen clinical outcomes.

ETHICS COMMITTEE APPROVAL

Institutional Ethics Committee approval was obtained from the ACEAS Independent Ethics Committee, Ahmedabad -380015 after submitting the clinical study documents (Product Information, PMCF protocol (AMS/ADVACRYL PLUS/2023 Ver. 01), CRF, etc.). The informed consent was waived on account of this being a retrospective study. Since ADVACRYL PLUS is a CE-certified device, the study was conducted as per the regulatory guidelines of EU MDR 2017/745. The study done as per the ICH – GCP, ICMR guidelines and New Drugs & Clinical Trials Rules 2019 (India).

ELIGIBILITY AND INCLUSION

The study was planned to include 200 subjects, we could not reach these numbers due to various reasons like less than expected sales, instability in our organization, etc. PMCF data of 103 Subjects was collected from January 2023 to December 2023.

All the subjects enrolled met the inclusion criteria in the study were included in this retrospective study:

Inclusion criteria

Patients who have been treated with ADVACRYL PLUS (Triclosan Coated Polyglactin 910) suture.

Exclusion criteria

Any patient who does not fulfil the inclusion criteria above.

Outcome measures/ endpoints

Primary Endpoint

- Number of Subjects presenting with wound complications [Time Frame: 03 months].
- Any wound disruption, wound dehiscence, fluid accumulation, and separation (Surgical Site Infection (SSI), Hematoma, Separation, Seroma, etc).

Secondary Endpoint

- Mean Operation Time in minutes [Time Frame: Intraoperative]
- Total procedure time [Time Frame: Intraoperative]
- Any Device Malfunction or Device Failure [Time Frame: Intra and Postoperative]

- Any Device Malfunction or Device Failure related to the use of ADVACRYL PLUS (based on the Investigator's Investigation for events not limited to Failure to perform or any other Malfunction when used in compliance with the Instructions for Use.)
- Length of Hospital Stay in days [Time Frame: From Postoperative through 03 month]
- Number of patients requiring Reoperation or Additional Surgical procedure [Time Frame: From Postoperative through 03 months]
- Number of patients presenting with Adverse Events related to the use of ADVACRYL PLUS surgical suture [Time Frame: From Postoperative through 03 months] (Any Adverse Events related to the use of ADVACRYL PLUS were based on the Investigator's Investigation.)
- Number of patients requiring Additional Surgical procedure resulting from Device malfunction, Device failure or any Adverse events [Time Frame: From Postoperative through 03 months]

All comer Subjects with ADVACRYL PLUS of any size or length were included in study and follow up for 3 months as per PMCF plan.

RESULTS AND DISCUSSION

Study Report

Data of 103 subjects was collected from different Surgeons and Hospitals collected from January 2023 till September 2023. 103 subjects' data were analyzed.

STUDY POPULATION: AGE, GENDER, MEDICAL AND TREATMENT HISTORY BASELINE CHARCTERISTICS

For Baseline Characteristics, the following attributes were studied.

1. Subjects' Age
2. Subjects' Gender
3. Medical History

Mean Age of the Study population age was 42.2 years with lowest age of 24 and highest age of 72, describe categories with 53 % of males and 47% of Females. 03 patients had medical history of diabetes mellitus, and 03 patients had hypertension and, 03 patient had medical history of both diabetes and hypertension.

Table 1: Gender distribution of the subjects

Gender	103 Subjects
Female	47%
Male	53%

Figure 1: Gender distribution of the subjects

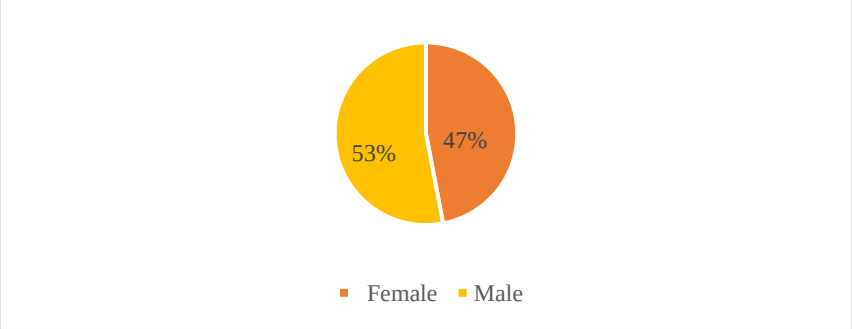


Table 2: Age categories

Age categories	103 Subjects
≤ 18 years	0%
Between 18 and 65 years	98%
≥ 65 years	2%

Figure 2: Age Categories

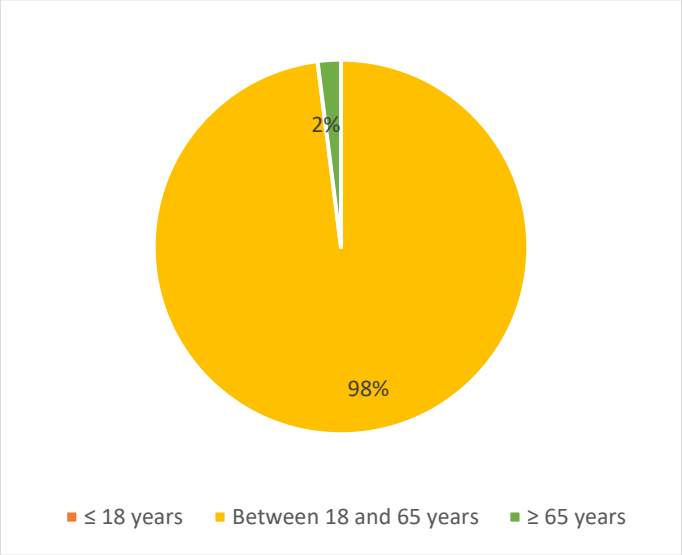
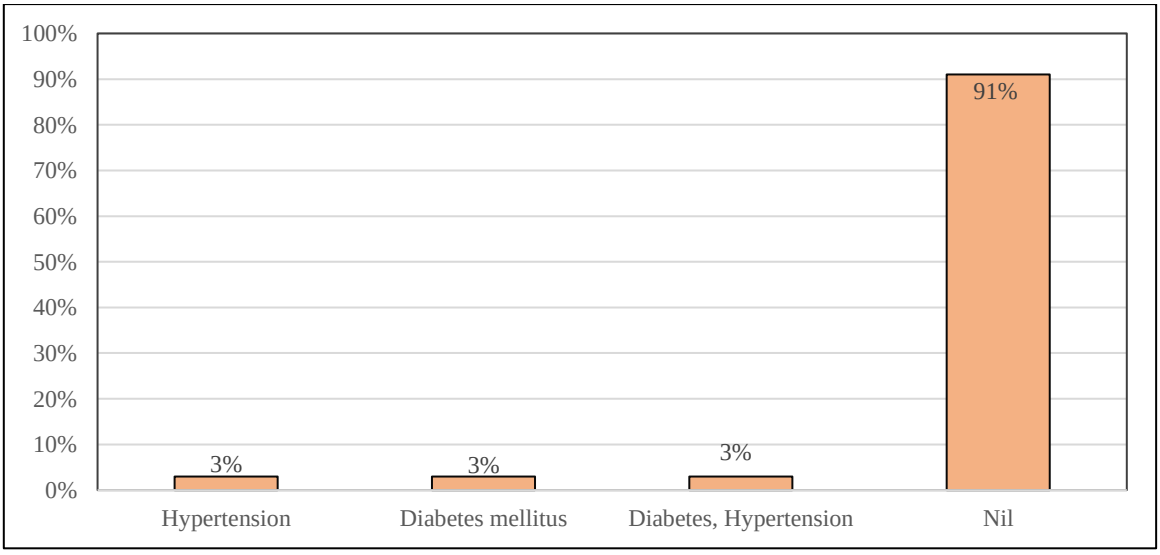


Table 3: Medical history of the subjects

Medical history	103 Subjects	Percentage
Hypertension	3	3%
Diabetes mellitus	3	3%
Diabetes, Hypertension	3	3%
Nil	94	91%

Figure 3: Medical history of the subjects



OPERATIVE DATA ANALYSIS

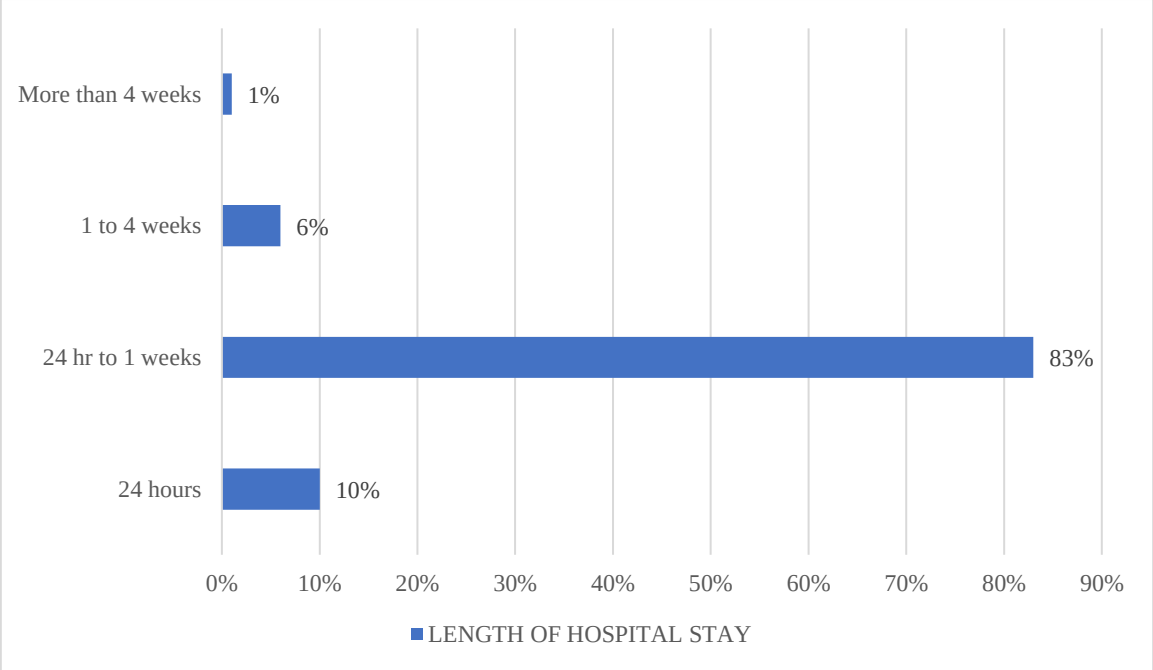
LENGTH OF HOSPITAL STAY

In total, the length of hospital stays of 83% of the subjects was 24 hours to 1 week, 10% was of 24 hours, 6% of 1 to 4 weeks, 1% of more than 4 weeks.

Table 4: Length of hospital stay

Length of Hospital Stay	103 Subjects	Percentage
24 hours	10	10%
24 hr to 1 weeks	86	83%
1 to 4 weeks	6	6%
More than 4 weeks	1	1%

Figure 4: Length of hospital stay



PATIENT BASELINE INFORMATION

CLINICAL PRESENTATION ON THE DAY 0

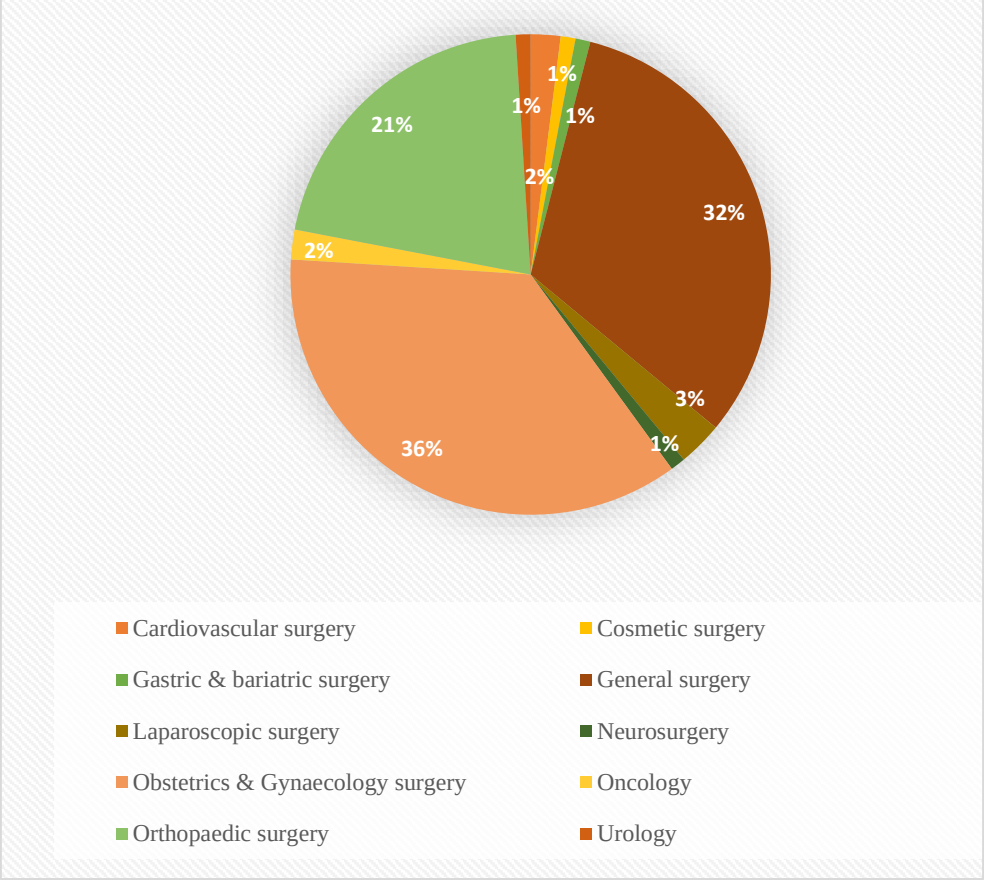
Of the 103 subjects, 32% of the Subjects underwent procedures in General Surgery, 36% in Obstetrics and Gynaecology Surgery, 21% in Orthopedic surgery, 3% in Laparoscopic surgery, 2% in Onco surgery, 2% in cardiovascular surgery, 1% in Cosmetic surgery, 1% in Gastric and Bariatric surgery and 1% in Neurosurgery.

STATICAL ANALYSIS: SURGERY

Table 5: List of surgical procedure where ADVACRYL PLUS was used

Surgery name	Number of subjects (103 subjects)	Percentage
Cardiovascular surgery	2	2%
Cosmetic surgery	1	1%
Gastric & bariatric surgery	1	1%
General surgery	33	32%
Laparoscopic surgery	3	3%
Neurosurgery	1	1%
Obstetrics & Gynaecology surgery	37	36%
Oncology	2	2%
Orthopaedic surgery	22	21%
Urology	1	1%

Figure 5: Percentage of procedures in various Surgical Categories



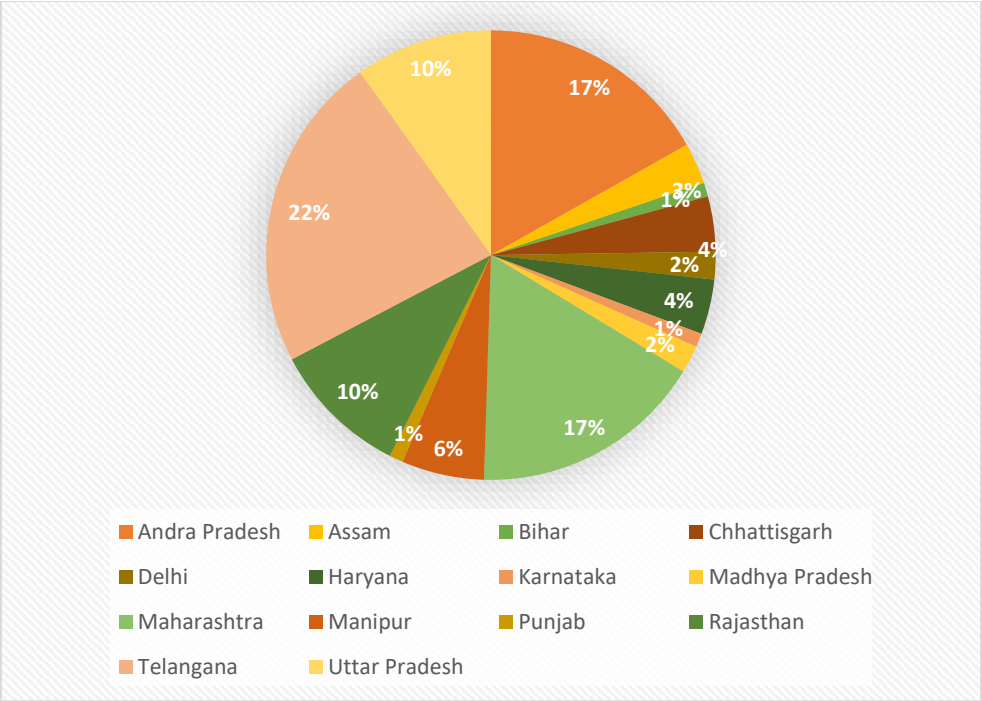
STATISTICAL ANALYSIS: STATE

In total, 23% of the Subjects from Telangana, 17% from Maharashtra, 17% from Andra Pradesh, 10% from Rajasthan, 10% from Uttar Pradesh, 4% from Chhattisgarh, 4% from Haryana, 3% from Assam, 2% from Madhya Pradesh, 2% from Delhi, 1% from Karnataka, 1% from Punjab, 6% from Manipur, 1% from Bihar.

Table 6: Number of subjects from different states

State	Number of Subjects (103 Subjects)	Percentage
Andra Pradesh	18	17%
Assam	3	3%
Bihar	1	1%
Chhattisgarh	4	4%
Delhi	2	2%
Haryana	4	4%
Karnataka	1	1%
Madhya Pradesh	2	2%
Maharashtra	17	17%
Manipur	6	6%
Punjab	1	1%
Rajasthan	10	10%
Telangana	24	23%
Uttar Pradesh	10	10%

Figure 6: Number of Subjects from different states



ADVACRYL PLUS HANDLING CHARACTERISTICS

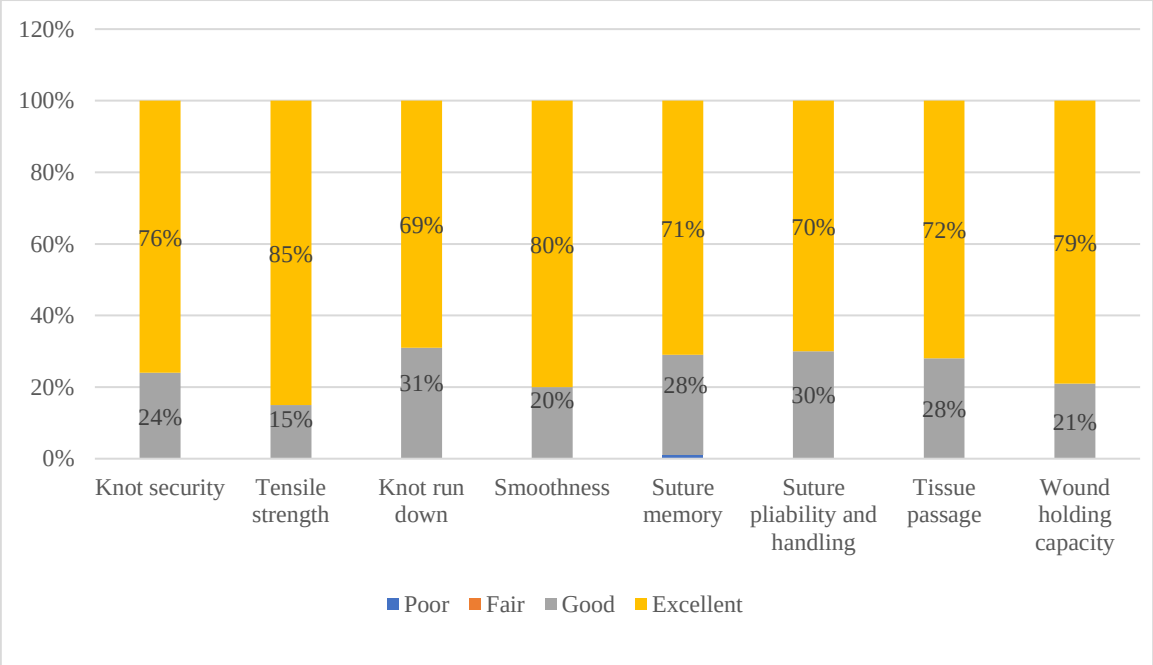
SUTURE PERFORMANCE

For Suture Performance, Knot Security, Tensile Strength, Knot Run Down, Smoothness, Suture Memory, Suture Pliability and Handling, Tissue Passage, and Wound Holding Capacity attributes were studied.

Table 7: Rating of Suture Performance attributes

103 Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Knot security	0%	0%	24%	76%
Tensile strength	0%	0%	15%	85%
Knot run down	0%	0%	31%	69%
Smoothness	0%	0%	20%	80%
Suture memory	1%	0%	28%	71%
Suture pliability and handling	0%	0%	30%	70%
Tissue passage	0%	0%	28%	72%
Wound holding capacity	0%	0%	21%	79%

Figure 7:Suture Performance attributes



NEEDLE PERFORMANCE

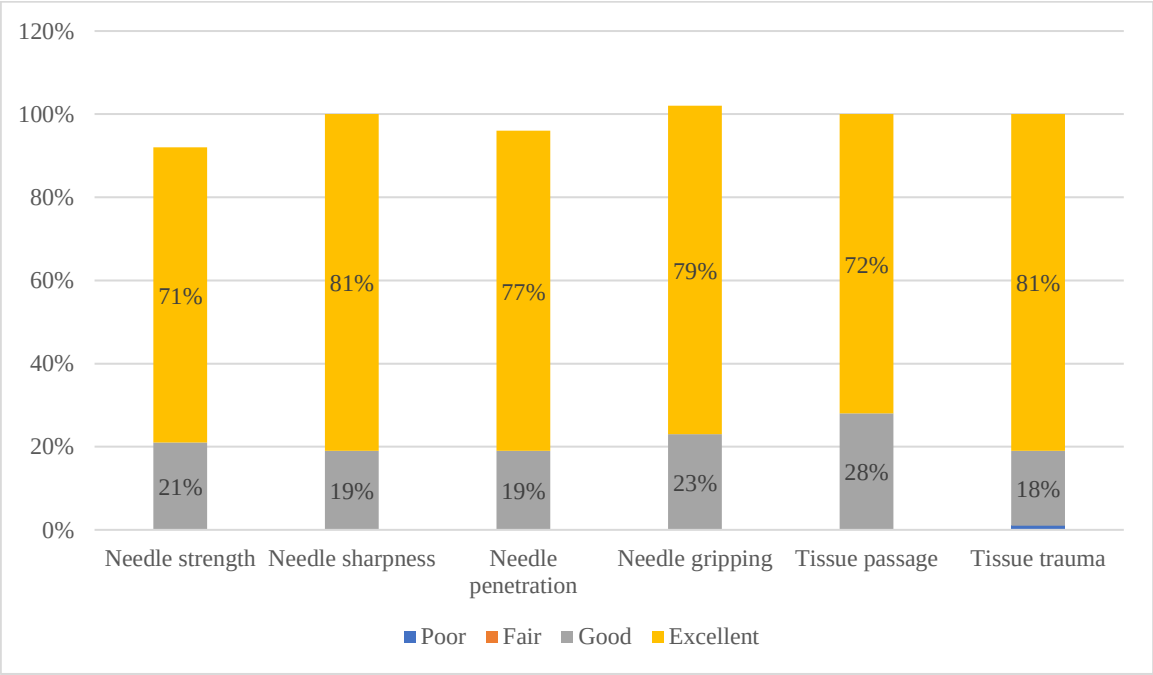
For needle performance like Needle strength, Needle sharpness, Needle penetration, Needle gripping, Tissue passage, and Tissue trauma were studied.

Table 8: Rating of Needle Performance attributes

103 Number of Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Needle strength	0%	0%	21%	71%
Needle sharpness	0%	0%	19%	81%
Needle penetration	0%	0%	19%	77%

Needle gripping	0%	0%	23%	79%
Tissue passage	0%	0%	28%	72%
Tissue trauma	1%	0%	18%	81%

Figure 8: Needle performance attributes



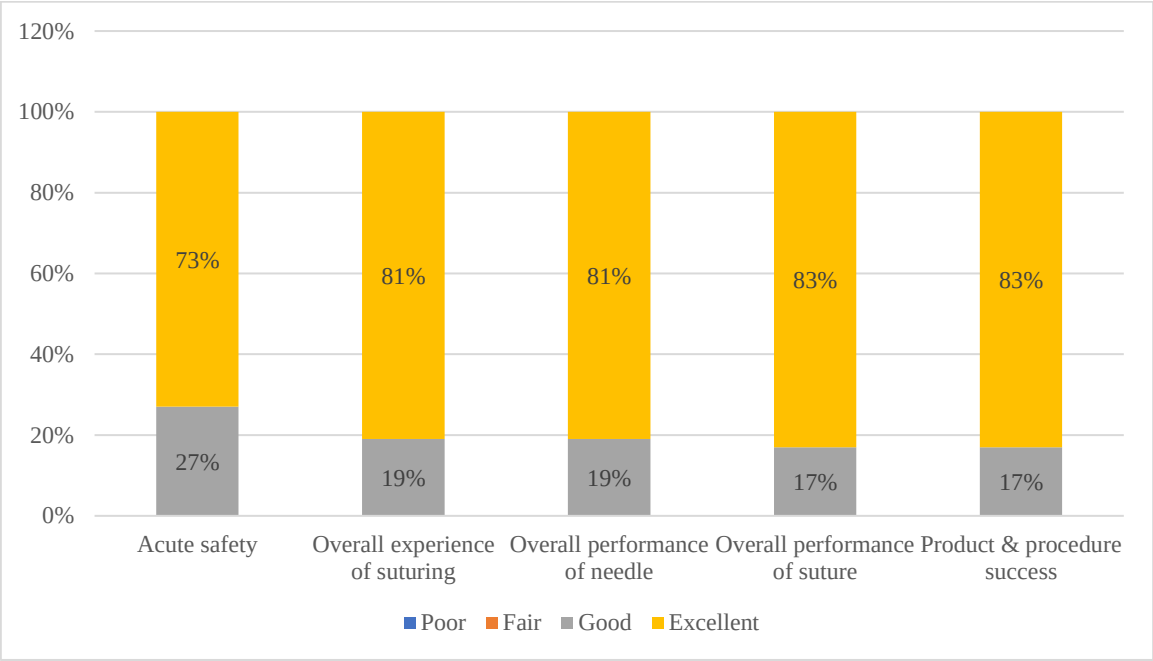
OVERALL PERFORMANCE

For Overall Performance of The Product, Acute Safety, Overall Experience of Suturing, Overall Performance of Needle, Overall Performance of Suture, Product & Procedure Success attributes were studied.

Table 9: Rating of Overall performance of the product

103 Number of Subjects analyzed				
Rating Category	**Poor**	**Fair**	**Good**	**Excellent**
Acute safety	0%	0%	27%	73%
Overall experience of suturing	0%	0%	19%	81%
Overall performance of needle	0%	0%	19%	81%
Overall performance of suture	0%	0%	17%	83%
Product & procedure success	0%	0%	17%	83%

Figure 9: Overall performance



CLINICAL PRESENTATION FOR THREE MONTHS FOLLOW UP DATA

At 3 months follow up, the following attributes were studied.

1. Tissue approximation
2. Wound complications like wound disruption, wound dehiscence, fluid accumulation, separation.
3. Suture Absorption time.
4. Details of adverse events/ serious adverse events

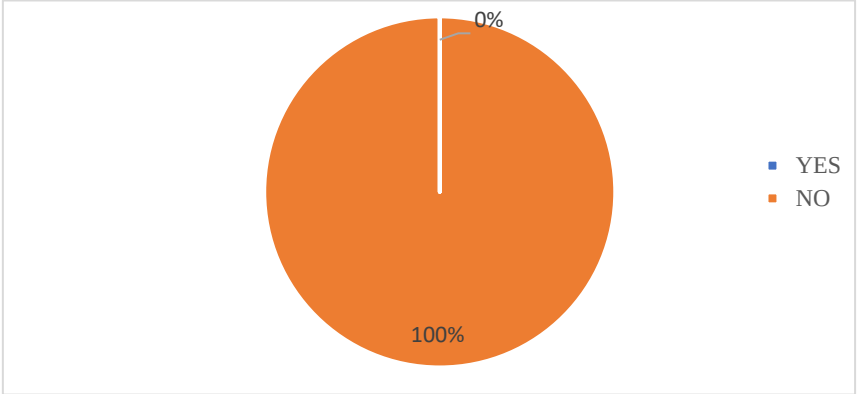
WOUND COMPLICATION

No wound complication was seen in any of the subjects at the end of 3 months follow up.

Table 10: Wound complication

Wound complication	103 Subjects
Yes	0%
No	100%

Figure 10: Wound Complication



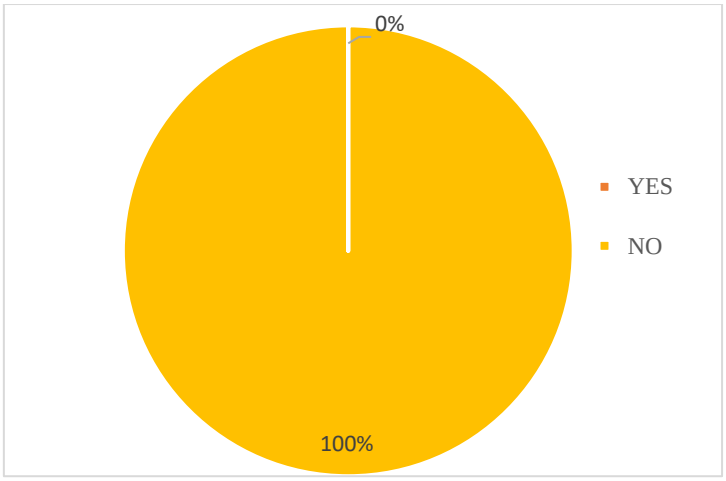
ADVERSE EVENTS (AE) OR SEVERE ADVERSE EVENTS (SAE):

In all the cases of clinical application in different surgical sites, there were no adverse events or severe adverse events reported on the day of operation or surgery and at 3 months follow up.

Table 11: Adverse reaction

Adverse reaction	103 Subjects
Yes	0%
No	100%

Figure 11:Adverse reaction



All the original tensile strength is lost between four to five weeks post implantation. Absorption of ADVACRYL PLUS is essentially complete up to 80 days.

LIMITATIONS

PMCF studies can suffer from limitations like limited data and subject selection bias. Best efforts to overcome these limitations were made by collecting sufficient data from an extremely high number of surgical centres across a wide geography and surgical specialties, by maintaining a high rate of follow-up data collection and analysing data with a very high standard of accuracy.

CONCLUSION

- In this real-world experience study in 103 subjects, ADVACRYL PLUS (Triclosan Coated Polyglactin 910) braided, synthetic absorbable sterile surgical sutures are used in a variety of surgical procedures. Follow-up data was obtained with a high rate of completion and high degree of accuracy.
- The study included subjects' data from >80 surgical centers across 14 different states of India, and included usage across 10 different surgical specialties, which demonstrates the wide diversity of clinical use of ADVACRYL PLUS (Triclosan Coated Polyglactin 910) sutures.
- The study successfully achieved its primary and secondary safety and performance objectives, over a significantly long 3-month follow-up period.
- ADVACRYL PLUS demonstrated excellent suture, needle and overall performance and were consistently rated excellent in surgeon's feedback across surgical specialties.

- No wound complications or adverse events were reported in this study during the follow-up period of 3 months, and there were no reports of prolonged or repeat hospitalization.
- ADVACRYL PLUS (Triclosan Coated Polyglactin 910) sutures are a safe and effective option for a very wide variety of surgical procedures in a diverse population.

Acknowledgements

We would like to thank the management of AMS Pvt. Ltd. For sponsoring this study. We express our heartfelt gratitude to the >80 surgical centers who contributed valuable subjects' data to this PMCF study.

Financial Disclosure statement

The study was sponsored by Advanced MedTech Solutions Pvt Ltd., Gujarat, India. No Financial remuneration or other benefits were paid to the hospitals or doctors contributing the subjects' data. The authors are full-time employees of Advanced MedTech Solutions Pvt. Ltd.

Conflict of Interest

No conflict of interest of any of the parties. Source documents can be made available on request.

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